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Requester's Full Name: Minnifield Examiner # : _____ Date: 7-1-03
Art Unit: 1645 Phone Number 305-3394 Serial Number: 09/830839
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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Tuberculosis Diagnostic Test

Inventors (please provide full names): Ajit. Lalvani
Ansar Pathan

Earliest Priority Filing Date: 11-04-98

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Seq. Search - SEQ1 + SEQ6

Pls. search inventor names

Pls search attached cls cls 27-43

Pls. return cls.

AA
1-15
6-15

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PTO-1590 (1-2000)

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L1            7 SEA FILE=CAPLUS ABB=ON  PLU=ON  LALVANI A?/AU AND PATHAN A?/AU


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L22           8 SEA FILE=MEDLINE ABB=ON  PLU=ON  LALVANI A?/AU AND PATHAN
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=> file embase; d que l41
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L41           8 SEA FILE=EMBASE ABB=ON  PLU=ON  LALVANI A?/AU AND PATHAN A?/AU
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
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RECORDS LAST ADDED: 16 July 2003 (20030716/ED)

L56          12 SEA FILE=BIOSIS ABB=ON  PLU=ON  LALVANI A?/AU AND PATHAN A?/AU


=> file wpid; d que l70
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MOST RECENT DERWENT UPDATE:     200346       <200346/DW>
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L70           2 SEA FILE=WPIDS ABB=ON  PLU=ON  LALVANI A?/AU AND PATHAN A?/AU


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PROCESSING COMPLETED FOR L56
PROCESSING COMPLETED FOR L70
L74 15 DUP REM L22 L1 L41 L56 L70 (22 DUPLICATES REMOVED)
ANSWERS '1-8' FROM FILE MEDLINE
ANSWERS '9-11' FROM FILE CAPLUS
ANSWERS '12-15' FROM FILE BIOSIS

=> d ibib ab l74 1-15

L74 ANSWER 1 OF 15 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002724225 MEDLINE
DOCUMENT NUMBER: 22328469 PubMed ID: 12441800
TITLE: Rapid detection of active and latent tuberculosis infection in HIV-positive individuals by enumeration of Mycobacterium tuberculosis-specific T cells.
AUTHOR: Chapman Ann L N; Munkanta Mwansa; Wilkinson Katalin A; **Pathan Ansar A**; Ewer Katie; Ayles Helen; Reece William H; Mwinga Alwyn; Godfrey-Faussett Peter; **Lalvani Ajit**
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK.
SOURCE: AIDS, (2002 Nov 22) 16 (17) 2285-93.
Journal code: 8710219. ISSN: 0269-9370.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021219
Last Updated on STN: 20030202
Entered Medline: 20030131

AB OBJECTIVES: An accurate test for Mycobacterium tuberculosis infection is urgently needed. The tuberculin skin test (TST) lacks sensitivity, particularly in HIV-infected individuals, and has poor specificity because of antigenic cross-reactivity with Bacillus Calmette-Guerin (BCG) vaccination. ESAT-6 and CFP-10 are antigens expressed in Mycobacterium tuberculosis, but not in Mycobacterium bovis BCG and most environmental mycobacteria. We investigated whether T cells specific for these antigens could serve as accurate markers of M. tuberculosis infection in an area of high tuberculosis and HIV prevalence. METHODS: Using the rapid ex-vivo enzyme-linked immunospot (ELISPOT) assay for IFN-gamma, we enumerated T cells specific for ESAT-6, CFP-10 and purified protein derivative (PPD) in blood samples from 50 Zambian tuberculosis patients, 75 healthy Zambian adults, and 40 healthy UK residents. TSTs were performed in 49 healthy Zambian adults. RESULTS: All (100%; n = 11) and 90% (n = 39) of HIV-negative and HIV-positive tuberculosis patients, respectively, had detectable ESAT-6- or CFP-10-specific T cells. The ESAT-6/CFP-10-based ELISPOT assay was positive in 37 out of 54 HIV-negative healthy Zambians, suggesting a 69% prevalence of latent M. tuberculosis infection. Fewer HIV-positive Zambians possessed ESAT-6/CFP-10-specific T cells, but the impact of HIV infection was less on this assay than on the PPD-based ELISPOT or TST. CONCLUSION: The ESAT-6/CFP-10-based ELISPOT assay detects active tuberculosis in HIV-positive individuals with high sensitivity. It is more specific, and possibly more sensitive, than PPD-based methods of detecting latent M. tuberculosis infection, and may potentially improve the targeting of isoniazid preventative therapy to HIV-positive

individuals with latent tuberculosis infection.

L74 ANSWER 2 OF 15 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001567381 MEDLINE
DOCUMENT NUMBER: 21528960 PubMed ID: 11673535
TITLE: Direct ex vivo analysis of antigen-specific IFN-gamma-secreting CD4 T cells in Mycobacterium tuberculosis-infected individuals: associations with clinical disease state and effect of treatment.
AUTHOR: **Pathan A A**; Wilkinson K A; Klenerman P; McShane H; Davidson R N; Pasvol G; Hill A V; **Lalvani A**
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom.
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Nov 1) 167 (9) 5217-25.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011024
Last Updated on STN: 20020122
Entered Medline: 20011205

AB The wide spectrum of clinical outcomes following infection with Mycobacterium tuberculosis is largely determined by the host immune response; therefore, we studied several clinically defined groups of individuals (n = 120) that differ in their ability to contain the bacillus. To quantitate M. tuberculosis-specific T cells directly ex vivo, we enumerated IFN-gamma-secreting CD4 T cells specific for ESAT-6, a secreted Ag that is highly specific for M. tuberculosis, and a target of protective immune responses in animal models. We found that frequencies of circulating ESAT-6 peptide-specific IFN-gamma-secreting CD4 T cells were higher in latently infected healthy contacts and subjects with minimal disease and low bacterial burdens than in patients with culture-positive active pulmonary tuberculosis ($p = 0.009$ and $p = 0.002$, respectively). Importantly, the frequency of these Ag-specific CD4 T cells fell progressively in all groups with treatment ($p = 0.005$), suggesting that the lower responses in patients with more extensive disease were not due to tuberculosis-induced immune suppression. This population of M. tuberculosis Ag-specific Th1-type CD4 T cells appears to correlate with clinical phenotype and declines during successful therapy; these features are consistent with a role for these T cells in the containment of M. tuberculosis in vivo. Such findings may assist in the design and evaluation of novel tuberculosis vaccine candidates.

L74 ANSWER 3 OF 15 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001380221 MEDLINE
DOCUMENT NUMBER: 21332031 PubMed ID: 11438135
TITLE: Enhanced contact tracing and spatial tracking of Mycobacterium tuberculosis infection by enumeration of antigen-specific T cells.
AUTHOR: **Lalvani A**; **Pathan A A**; Durkan H; Wilkinson K A; Whelan A; Deeks J J; Reece W H; Latif M; Pasvol G; Hill A V
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, UK.. ajit.lalvani@ndm.ox.ac.uk
SOURCE: LANCET, (2001 Jun 23) 357 (9273) 2017-21.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712

AB BACKGROUND: Identification of individuals latently infected with Mycobacterium tuberculosis is an important part of tuberculosis control. The current method, the tuberculin skin test (TST), has poor specificity because of the antigenic cross-reactivity of purified protein derivative (PPD) with M bovis BCG vaccine and environmental mycobacteria. ESAT-6 is a secreted antigen that is highly specific for M tuberculosis complex, but is absent from M bovis BCG. With an enzyme-linked immunospot (ELISPOT) assay for interferon gamma, we have identified ESAT-6-specific T cells as an accurate marker of M tuberculosis infection. METHODS: We did a prospective, masked study of 50 healthy contacts, with varying but well defined degrees of exposure to M tuberculosis, who attended an urban contact-tracing clinic. We assessed and compared the efficacy of our assay and TST for detection of symptomless infected individuals by correlation of test results with the degree of exposure to an infectious index case. FINDINGS: The ESAT-6 ELISPOT assay results had a strong positive relation with increasing intensity of exposure (odds ratio=9.0 per unit increase in level of exposure [95% CI 2.6--31.6], p=0.001), whereas TST results had a weaker relation with exposure (1.9 [1.0--3.5], p=0.05). By contrast, ELISPOT results were not correlated with BCG vaccination status (p=0.7), whereas TST results were significantly more likely to be positive in BCG-vaccinated contacts (12.1 [1.3--115.7], p=0.03). INTERPRETATION: This new antigen-specific T cell-based assay could allow more accurate identification of symptom-free individuals recently exposed to M tuberculosis, and thereby help to improve tuberculosis control.

L74 ANSWER 4 OF 15 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001271748 MEDLINE
DOCUMENT NUMBER: 21179912 PubMed ID: 11282752
TITLE: Rapid detection of Mycobacterium tuberculosis infection by enumeration of antigen-specific T cells.
COMMENT: Comment in: Am J Respir Crit Care Med. 2001 Mar;163(4):807-8
Comment in: Am J Respir Crit Care Med. 2002 May 15;165(10):1452; discussion 1452
AUTHOR: **Lalvani A; Pathan A A;** McShane H; Wilkinson R J; Latif M; Conlon C P; Pasvol G; Hill A V
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom.. ajit.lalvani@ndm.ox.ac.uk
SOURCE: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, (2001 Mar) 163 (4) 824-8.
Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20021217
Entered Medline: 20010521

AB There is no reliable means of detecting latent M. tuberculosis infection,

and even in patients with active tuberculosis, infection is often unconfirmed. We hypothesized that M. tuberculosis antigen-specific T cells might reliably indicate infection. We enumerated peripheral blood-derived interferon gamma (IFN-gamma)-secreting T cells responding to epitopes from ESAT-6, an antigen that is highly specific for M. tuberculosis complex but absent from BCG, in four groups of individuals. Forty-five of 47 patients with bacteriologically confirmed tuberculosis had ESAT-6-specific IFN-gamma-secreting T cells, compared with four of 47 patients with nontuberculous illnesses, indicating that these T cells are an accurate marker of M. tuberculosis infection. This assay thus has a sensitivity of 96% (95% confidence interval [CI] 92-100) for detecting M. tuberculosis infection in this patient population. By comparison, of the 26 patients with tuberculosis who had a diagnostic tuberculin skin test (TST), only 18 (69%) were positive (p = 0.003). In addition, 22 of 26 (85%) TST-positive exposed household contacts had ESAT-6-specific T cells, whereas zero of 26 unexposed BCG-vaccinated subjects responded. This approach enables rapid detection of M. tuberculosis infection in patients with active tuberculosis and in exposed asymptomatic individuals at high risk of latent infection; it also successfully distinguishes between M. tuberculosis infection and BCG vaccination. This capability may facilitate tuberculosis control in nonendemic regions.

L74 ANSWER 5 OF 15 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001125769 MEDLINE
DOCUMENT NUMBER: 21064969 PubMed ID: 11133379
TITLE: Enumeration of T cells specific for RD1-encoded antigens suggests a high prevalence of latent Mycobacterium tuberculosis infection in healthy urban Indians.
COMMENT: Comment in: J Infect Dis. 2001 Dec 1;184(11):1497-8
AUTHOR: **Lalvani A**; Nagvenkar P; Udwadia Z; **Pathan A A**; Wilkinson K A; Shastri J S; Ewer K; Hill A V; Mehta A; Rodrigues C
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom.. ajit.lalvani@ndm.ox.ac.uk
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (2001 Feb 1) 183 (3) 469-77.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20030105
Entered Medline: 20010222

AB Knowledge of the prevalence of latent Mycobacterium tuberculosis infection is crucial for effective tuberculosis control, but tuberculin skin test surveys have major limitations, including poor specificity because of the broad antigenic cross-reactivity of tuberculin. The M. tuberculosis RD1 genomic segment encodes proteins, such as early secretory antigenic target (ESAT)-6, that are absent from M. bovis bacille Calmette-Guerin (BCG) and most environmental mycobacteria. We recently identified circulating ESAT-6-specific T cells as an accurate marker of M. tuberculosis infection. Here, interferon-gamma-secreting T cells specific for peptides derived from ESAT-6 and a second RD1 gene product, CFP10, were enumerated in 100 prospectively recruited healthy adults in Bombay (Mumbai), India. Eighty percent responded to >/=1 antigen, and many donors had high frequencies of T cells that were specific for certain immunodominant peptides. In contrast, of 40 mostly BCG-vaccinated, United Kingdom-resident healthy adults, none responded to either antigen. This

study suggests an 80% prevalence of latent M. tuberculosis infection in urban India.

L74 ANSWER 6 OF 15 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2000452726 MEDLINE
DOCUMENT NUMBER: 20462631 PubMed ID: 11009107
TITLE: High frequencies of circulating IFN-gamma-secreting CD8 cytotoxic T cells specific for a novel MHC class I-restricted Mycobacterium tuberculosis epitope in M. tuberculosis-infected subjects without disease.
AUTHOR: **Pathan A A**; Wilkinson K A; Wilkinson R J; Latif M; McShane H; Pasvol G; Hill A V; **Lalvani A**
CORPORATE SOURCE: Institute of Molecular Medicine, Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, GB.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (2000 Sep) 30 (9) 2713-21. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001012

AB MHC class I-restricted CD8 cytotoxic T lymphocytes (CTL) are essential for protective immunity to Mycobacterium tuberculosis in animal models but their role in humans remains unclear. We therefore studied subjects who had successfully contained M. tuberculosis infection in vivo, i.e. exposed healthy household contacts and individuals with inactive self-healed pulmonary tuberculosis. Using the ELISPOT assay for IFN-gamma, we screened peptides from ESAT-6, a secreted antigen that is highly specific for M. tuberculosis. We identified a novel nonamer epitope: unstimulated peripheral blood-derived CD8 T cells displayed peptide-specific IFN-gamma release ex vivo while CD8 T cell lines and clones exhibited HLA-A68.02-restricted cytolytic activity and recognized endogenously processed antigen. The frequency of CD8 CTL specific for this single M. tuberculosis epitope, 1/2500 peripheral blood lymphocytes, was equivalent to the combined frequency of all IFN-gamma-secreting purified protein derivative-reactive T cells ex vivo. This highly focused CTL response was maintained in an asymptomatic contact over 2 years and is the most potent antigen-specific antimycobacterial CD8 CTL response hitherto described. Thus, human M. tuberculosis-specific CD8 CTL are not necessarily associated with active disease per se. Rather, our results are consistent with a protective role for these ESAT-6-specific CD8 T cells in the long-term control of M. tuberculosis in vivo in humans.

L74 ANSWER 7 OF 15 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1999445635 MEDLINE
DOCUMENT NUMBER: 99445635 PubMed ID: 10515829
TITLE: Potent induction of focused Th1-type cellular and humoral immune responses by RTS,S/SBAS2, a recombinant Plasmodium falciparum malaria vaccine.
AUTHOR: **Lalvani A**; Moris P; Voss G; **Pathan A A**; Kester K E; Brookes R; Lee E; Koutsoukos M; Plebanski M; Delchambre M; Flanagan K L; Carton C; Slaoui M; Van Hoecke C; Ballou W R; Hill A V; Cohen J
CORPORATE SOURCE: Nuffield Dept. of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom. ajit.lalvani@ndm. ox.ac.uk.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1999 Nov) 180 (5) 1656-64.

Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991209

AB The RTS,S/SBAS2 vaccine confers sterile protection against Plasmodium falciparum sporozoite challenge. The mechanisms underlying this are of great interest, yet little is known about the immune effector mechanisms induced by this vaccine. The immune responses induced by RTS,S/SBAS2 were characterized in 10 malaria-naive volunteers. Several epitopes in the circumsporozoite protein (CSP) were identified as targets of cultured interferon (IFN)-gamma-secreting CD4+ T cells. RTS,S-specific IFN-gamma-secreting effector T cells were induced in 8 subjects; this ex vivo response mapped to a single peptide in Th2R. CSP-specific CD8+ cytotoxic T lymphocytes were not detected. RTS, S-specific IFN-gamma production was universal, whereas interleukin-4 and -5 production was rare. RTS,S-specific lymphoproliferative responses and antibodies to CSP were strongly induced in all volunteers. Responses waned with time but were boostable. Thus, RTS, S/SBAS2 is a potent inducer of Th1-type cellular and humoral immunity. These results highlight possible immune mechanisms of protection and have important implications for vaccine design in general.

L74 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1998081863 MEDLINE
DOCUMENT NUMBER: 98081863 PubMed ID: 9419365
TITLE: Human cytolytic and interferon gamma-secreting CD8+ T lymphocytes specific for Mycobacterium tuberculosis.
AUTHOR: **Lalvani A**; Brookes R; Wilkinson R J; Malin A S; **Pathan A A**; Andersen P; Dockrell H; Pasvol G; Hill A V
CORPORATE SOURCE: Molecular Immunology Group, Institute of Molecular Medicine, Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Jan 6) 95 (1) 270-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980218

AB Protective immunity to Mycobacterium tuberculosis is poorly understood, but mounting evidence, at least in animal models, implicates major histocompatibility complex class I-restricted CD8+ T cells as an essential component. By using a highly sensitive assay for single cell interferon gamma release, we screened an array of M. tuberculosis antigen-derived peptides congruent with HLA class I allele-specific motifs. We identified CD8+ T cells specific for epitopes in the early secretory antigenic target 6 during active tuberculosis, after clinical recovery and in healthy contacts. Unrestimulated cells exhibited peptide-specific interferon gamma secretion, whereas lines or clones recognized endogenously processed

antigen and showed cytolytic activity. These results provide direct evidence for the involvement of CD8+ cytotoxic T lymphocytes in host defense against M. tuberculosis in humans and support current attempts to generate protective cytotoxic T lymphocyte responses against M. tuberculosis by vaccination.

L74 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:716868 CAPLUS
DOCUMENT NUMBER: 137:246533
TITLE: Mycobacterium tuberculosis epitopes in vaccines and detection of mycobacterial-specific cytotoxic T-cells
INVENTOR(S): **Lalvani, Ajit; Pathan, Ansar A.;** Hill, Adrian V. S.
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Ser. No. 467,893, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002131976	A1	20020919	US 2001-916201	20010727
PRIORITY APPLN. INFO.:			US 1998-113783P P	19981223
			US 1999-467893 B2	19991221

AB A method of detecting an anti-mycobacterial CD8 T cell response comprising contacting a population of CD8 T cells of an individual with one or more peptides selected from the peptides represented by SEQ ID NO: 3, 4, 7, 8, 9, 10, 11 or 12, and, optionally, one or two further peptides represented by SEQ ID NO: 1 and/or 2, wherein one or more of said peptides may be substituted by an analog which binds a T cell receptor which recognizes the corresponding substituted peptide, and detg. whether CD8 T cells of the CD8 T cell population recognize the peptide(s). The invention also provides a method of vaccinating against infection by a mycobacterium, wherein the vaccination leads to a CD8 T cell response, comprising administering (i) a CD8 T cell epitope of a mycobacterium protein, (ii) an analog of the epitope which is capable of inhibiting the binding of the epitope to a T cell receptor, (iii) a precursor or (i) or (ii) which is capable of being processed to provide (i) or (ii), or (iv) a polynucleotide which is capable of being expressed to provide (i), (ii) or (iii). The method of detecting CD8 T cells is an ELISPOT assay which detects interferon-.gamma., released by the T cells following peptide recognition, using an immobilized anti-IFN-.gamma. antibody.

L74 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 7
ACCESSION NUMBER: 2000:314729 CAPLUS
DOCUMENT NUMBER: 132:320929
TITLE: Test for diagnosis of tuberculosis
INVENTOR(S): **Lalvani, Ajit; Pathan, Ansar Ahmed**
PATENT ASSIGNEE(S): Isis Innovation Limited, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000026248 A2 20000511 WO 1999-GB3635 19991103
WO 2000026248 A3 20011011
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9964809 A1 20000522 AU 1999-64809 19991103
BR 9915055 A 20010807 BR 1999-15055 19991103
EP 1144447 A2 20011017 EP 1999-952697 19991103
EP 1144447 A3 20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002532064 T2 20021002 JP 2000-579635 19991103
PRIORITY APPLN. INFO.: GB 1998-24213 A 19981104
US 1998-107004P P 19981104
WO 1999-GB3635 W 19991103

AB The authors disclose a method of diagnosing infection or exposure to Mycobacterium tuberculosis. The method is comprised of (1) contacting a population of T cells from the host with one or more peptides or peptide analogs derived from ESAT-6 and (2) detg. whether the T cells recognize the peptide(s) and/or analog(s) using ELISPOT.

L74 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 11
ACCESSION NUMBER: 1998:73086 CAPLUS
DOCUMENT NUMBER: 128:191348
TITLE: Optimization of a peptide-based protocol employing IL-7 for in vitro restimulation of human cytotoxic T lymphocyte precursors
AUTHOR(S): **Lalvani, Ajit**; Dong, Tao; Ogg, Graham; **Pathan, Ansar A.**; Newell, Heidi; Hill, Adrian V. S.; McMichael, Andrew J.; Rowland-Jones, Sarah
CORPORATE SOURCE: Institute of Molecular Medicine, Molecular Immunology Group, University of Oxford, Oxford, OX3 9DU, UK
SOURCE: Journal of Immunological Methods (1997), 210(1), 65-77
CODEN: JIMMBG; ISSN: 0022-1759
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A variety of different methods for the in vitro restimulation of human cytotoxic T lymphocyte (CTL) precursors (CTLp) are in use. The authors' aim was to enhance the detection of circulating human CTLp in peripheral blood. The authors have developed a standardized and highly efficient method for restimulating CTLp. Synthetic peptides were used to restimulate cognate CTLp from peripheral blood mononuclear cells (PBMC), and effector CTL capable of lysing peptide-pulsed and virus infected targets were generated. The effects of several parameters on CTL specific for influenza A, EBV and HIV-1 were evaluated, and the optimum peptide concn. for CTL generation was established. Supplementation of initial cultures with IL-7 greatly enhanced peptide-specific lytic activity for all peptides tested and the dose-response relation for IL-7 was delineated. A novel technique using peptide-MHC class I mol. tetramers to stain T cells bearing cognate T cell receptors permitted enumeration of antigen-specific CD8+ CTL during in vitro restimulation; IL-7 supplementation selectively expanded the population of peptide-specific CD8+ CTL. Importantly, this protocol, while enhancing the restimulation and lytic activity of secondary CTL, does not induce primary CTL in vitro.

The improved efficiency with which CTL are generated in this system substantially enhances the sensitivity of CTL culture and the 51Cr release assay to detect low levels of CTL activity.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 12 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:131124 BIOSIS
DOCUMENT NUMBER: PREV199900131124
TITLE: Identification of conserved, CD8+ cytotoxic T cell epitopes in ESAT-6, a tuberculosis vaccine candidate.
AUTHOR(S): **Pathan, A. (1)**; Brookes, R. (1); Pritchard, H. (1); Wilkinson, R.; Pasvol, G.; Hill, A. (1); **Lalvani, A. (1)**
CORPORATE SOURCE: (1) Nuffield Dep. Clin. Med., John Radcliffe Hosp., Oxford UK
SOURCE: Immunology, (Dec., 1998) Vol. 95, No. SUPPL. 1, pp. 108. Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998 ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L74 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:112697 BIOSIS
DOCUMENT NUMBER: PREV199900112697
TITLE: Human T cell responses to the antigen ESAT-6 characterize a vaccine candidate and potential diagnostic test for tuberculosis.
AUTHOR(S): **Pathan, A. (1)**; Brookes, R. (1); Pritchard, H. (1); Wilkinson, R.; Pasvol, G.; Hill, A. (1); **Lalvani, A. (1)**
CORPORATE SOURCE: (1) Nuffield Dep. Clinical Med., John Radcliffe Hosp., Oxford UK
SOURCE: Immunology, (Dec., 1998) Vol. 95, No. SUPPL. 1, pp. 90. Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998 ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L74 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:107282 BIOSIS
DOCUMENT NUMBER: PREV199800107282
TITLE: Human cytolytic CD8+ T lymphocytes specific for Mycobacterium tuberculosis.
AUTHOR(S): Brookes, R. (1); **Lalvani, A. (1)**; Wilkinson, R.; **Pathan, A. (1)**; Malin, A.; Andersen, P.; Dockrell, H.; Pasvol, G.; Hill, A. V. S. (1)
CORPORATE SOURCE: (1) NDM, John Radcliffe Hosp., Oxford OX3 9DU UK
SOURCE: Immunology, (Dec., 1997) Vol. 92, No. SUPPL. 1, pp. 77. Meeting Info.: 5th Annual Congress of the British Society for Immunology Brighton, England, UK December 2-5, 1997 British Society for Immunology ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L74 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:107187 BIOSIS
DOCUMENT NUMBER: PREV199800107187

TITLE: Correlation of protective immunity in tuberculosis patients and healthy contacts.
AUTHOR(S): **Pathan, A. A. (1); Lalvani, A. (1);** Brookes, R. (1); Wilkinson, R.; Pasvol, G.; Hill, A. V. S.
CORPORATE SOURCE: (1) NDM, John Radcliffe Hosp., Oxford OX3 9DU UK
SOURCE: Immunology, (Dec., 1997) Vol. 92, No. SUPPL. 1, pp. 58. Meeting Info.: 5th Annual Congress of the British Society for Immunology Brighton, England, UK December 2-5, 1997 British Society for Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

=> file caplus; d que l10; d que l19
FILE 'CAPLUS' ENTERED AT 13:18:46 ON 21 JUL 2003
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FILE COVERS 1907 - 21 Jul 2003 VOL 139 ISS 4
FILE LAST UPDATED: 20 Jul 2003 (20030720/ED)

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L2	8921	SEA	FILE=CAPLUS ABB=ON	PLU=ON	TUBERCULOSIS/CT
L3	2926	SEA	FILE=CAPLUS ABB=ON	PLU=ON	TUBERCULOSTATICS/CT
L4	5979	SEA	FILE=CAPLUS ABB=ON	PLU=ON	ANTITUBERC?
L5	44404	SEA	FILE=CAPLUS ABB=ON	PLU=ON	DIAGNOSIS+NT/CT
L6	112861	SEA	FILE=CAPLUS ABB=ON	PLU=ON	PEPTIDES/CW
L9	455	SEA	FILE=CAPLUS ABB=ON	PLU=ON	L5 (L) TUBERCUL?
L10	17	SEA	FILE=CAPLUS ABB=ON	PLU=ON	(L2 OR L3 OR L4) AND L9 AND L6

L14	50170	SEA	FILE=CAPLUS ABB=ON	PLU=ON	T-CELL/CW
L15	205	SEA	FILE=CAPLUS ABB=ON	PLU=ON	L14 (10A) (TUBERCULOSIS)
L16	261	SEA	FILE=CAPLUS ABB=ON	PLU=ON	L14 (10A) (DIAGNOS?)
L17	5	SEA	FILE=CAPLUS ABB=ON	PLU=ON	L15 AND L16
L18	1193455	SEA	FILE=CAPLUS ABB=ON	PLU=ON	PROTEINS OR PEPTIDES
L19	1	SEA	FILE=CAPLUS ABB=ON	PLU=ON	L17 AND L18

=> s (l10 or l19) not l1 L1 = authors previously displayed
L75 17 (L10 OR L19) NOT L1

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=> file medline; d que l32; d que l35
FILE 'MEDLINE' ENTERED AT 13:19:35 ON 21 JUL 2003

 FILE LAST UPDATED: 19 JUL 2003 (20030719/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L23       18265 SEA FILE=MEDLINE ABB=ON  PLU=ON  TUBERCULOSIS+NT/CT (L) DI/CT
L24      866080 SEA FILE=MEDLINE ABB=ON  PLU=ON  PEPTIDES+NT/CT
L28       10048 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23/MAJ
L30      150584 SEA FILE=MEDLINE ABB=ON  PLU=ON  T CELL
L32          13 SEA FILE=MEDLINE ABB=ON  PLU=ON  L28 AND L24 AND L30



L23       18265 SEA FILE=MEDLINE ABB=ON  PLU=ON  TUBERCULOSIS+NT/CT (L) DI/CT
L24      866080 SEA FILE=MEDLINE ABB=ON  PLU=ON  PEPTIDES+NT/CT
L28       10048 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23/MAJ
L30      150584 SEA FILE=MEDLINE ABB=ON  PLU=ON  T CELL
L31          22 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L24 AND L30
L32          13 SEA FILE=MEDLINE ABB=ON  PLU=ON  L28 AND L24 AND L30
L33           9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L31 NOT L32
L34        1197 SEA FILE=MEDLINE ABB=ON  PLU=ON  TUBERCULOSIS, BOVINE/CT
L35           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L33 AND L34

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L76          15 (L32 OR L35) NOT L22

=> file embase; d que l45; d que l51
FILE 'EMBASE' ENTERED AT 13:20:31 ON 21 JUL 2003
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 FILE COVERS 1974 TO 17 Jul 2003 (20030717/ED)

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L37       10237 SEA FILE=EMBASE ABB=ON  PLU=ON  TUBERCULOSIS+NT/CT (L)
                DIAGNOSIS
L38        8758 SEA FILE=EMBASE ABB=ON  PLU=ON  L37/MAJ
L40       91601 SEA FILE=EMBASE ABB=ON  PLU=ON  T LYMPHOCYTE/CT
L44        2475 SEA FILE=EMBASE ABB=ON  PLU=ON  MYCOBACTERIUM BOVIS/CT
L45           5 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 AND L40 AND L44



L37       10237 SEA FILE=EMBASE ABB=ON  PLU=ON  TUBERCULOSIS+NT/CT (L)
                DIAGNOSIS
L38        8758 SEA FILE=EMBASE ABB=ON  PLU=ON  L37/MAJ
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L39       18609 SEA FILE=EMBASE ABB=ON  PLU=ON  PEPTIDE/CT
L44        2475 SEA FILE=EMBASE ABB=ON  PLU=ON  MYCOBACTERIUM BOVIS/CT
L49        1417 SEA FILE=EMBASE ABB=ON  PLU=ON  L44/MAJ
L51           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 AND L39 AND L49

=> s (l45 or l51) not l41  L41 = authors, previously displayed
L77           6 (L45 OR L51) NOT L41

=> file biosis; d que l57
FILE 'BIOSIS' ENTERED AT 13:21:01 ON 21 JUL 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 16 July 2003 (20030716/ED)


L52        4566 SEA FILE=BIOSIS ABB=ON  PLU=ON  TUBERCULOSIS (10A) DIAGNOSIS
L53      234686 SEA FILE=BIOSIS ABB=ON  PLU=ON  T (W) (CELL OR LYMPHOCYTE)
L54      290103 SEA FILE=BIOSIS ABB=ON  PLU=ON  PEPTIDE
L55           8 SEA FILE=BIOSIS ABB=ON  PLU=ON  L52 AND L53 AND L54
L57           6 SEA FILE=BIOSIS ABB=ON  PLU=ON  L55 NOT CLON?/TI

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L78           6 L57 NOT L56

=> file wpid; d que l73
FILE 'WPIDS' ENTERED AT 13:21:31 ON 21 JUL 2003
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FILE LAST UPDATED:          19 JUL 2003      <20030719/UP>
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    GUIDES, PLEASE VISIT:
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L58        3236 SEA FILE=WPIDS ABB=ON  PLU=ON  TUBERCULOSIS
L60       49361 SEA FILE=WPIDS ABB=ON  PLU=ON  DIAGNOSIS
L61      133342 SEA FILE=WPIDS ABB=ON  PLU=ON  PEPTIDE OR PROTEIN
L63        2949 SEA FILE=WPIDS ABB=ON  PLU=ON  MYCOBACTER?
L72      379093 SEA FILE=WPIDS ABB=ON  PLU=ON  TEST? OR ASSAY?
L73          25 SEA FILE=WPIDS ABB=ON  PLU=ON  L58 (10A) L60 AND L63 AND L61
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AND L72

=> s l73 not l70 L70 = authors, previously displayed
L79 25 L73 NOT L70

=> dup rem l76 l75 l77 l78 l79
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PROCESSING COMPLETED FOR L76
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PROCESSING COMPLETED FOR L77
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L79
L80 62 DUP REM L76 L75 L77 L78 L79 (7 DUPLICATES REMOVED)
ANSWERS '1-15' FROM FILE MEDLINE
ANSWERS '16-31' FROM FILE CAPLUS
ANSWERS '32-35' FROM FILE EMBASE
ANSWERS '36-39' FROM FILE BIOSIS
ANSWERS '40-62' FROM FILE WPIDS

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L80 ANSWER 1 OF 62 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001638720 MEDLINE
DOCUMENT NUMBER: 21546626 PubMed ID: 11687445
TITLE: Tuberculin skin testing compared with **T-cell** responses to Mycobacterium tuberculosis-specific and nonspecific antigens for detection of latent infection in persons with recent tuberculosis contact.
AUTHOR: Arend S M; Engelhard A C; Groot G; de Boer K; Andersen P; Ottenhoff T H; van Dissel J T
CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands.. s.m.arend@lumc.nl
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2001 Nov) 8 (6) 1089-96.
Journal code: 9421292. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020128
Entered Medline: 20020125
AB The tuberculin skin test (TST) is used for the identification of latent tuberculosis (TB) infection (LTBI) but lacks specificity in Mycobacterium

bovis BCG-vaccinated individuals, who constitute an increasing proportion of TB patients and their contacts from regions where TB is endemic. In previous studies, **T-cell** responses to ESAT-6 and CFP-10, M. tuberculosis-specific antigens that are absent from BCG, were sensitive and specific for detection of active TB. We studied 44 close contacts of a patient with smear-positive pulmonary TB and compared the standard screening procedure for LTBI by TST or chest radiographs with **T-cell** responses to M. tuberculosis-specific and nonspecific antigens. Peripheral blood mononuclear cells were cocultured with ESAT-6, CFP-10, TB10.4 (each as recombinant antigen and as a mixture of overlapping synthetic peptides), M. tuberculosis sonicate, purified protein derivative (PPD), and short-term culture filtrate, using gamma interferon production as the response measure. LTBI screening was by TST in 36 participants and by chest radiographs in 8 persons. Nineteen contacts were categorized as TST negative, 12 were categorized as TST positive, and 5 had indeterminate TST results. Recombinant antigens and peptide mixtures gave similar results. Responses to TB10.4 were neither sensitive nor specific for LTBI. **T-cell** responses to ESAT-6 and CFP-10 were less sensitive for detection of LTBI than those to PPD (67 versus 100%) but considerably more specific (100 versus 72%). The specificity of the TST or in vitro responses to PPD will be even less when the proportion of BCG-vaccinated persons among TB contacts evaluated for LTBI increases.

L80 ANSWER 2 OF 62 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001410275 MEDLINE
DOCUMENT NUMBER: 21229296 PubMed ID: 11329460
TITLE: Use of synthetic peptides derived from the antigens ESAT-6 and CFP-10 for differential diagnosis of bovine tuberculosis in cattle.
AUTHOR: Vordermeier H M; Whelan A; Cockle P J; Farrant L; Palmer N; Hewinson R G
CORPORATE SOURCE: TB Research Group, Department of Bacterial Diseases, Veterinary Laboratories Agency-Weybridge, New Haw, Addlestone KT15 3NB, United Kingdom..
mvordermeier.vla@gtnet.gov.uk
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2001 May) 8 (3) 571-8.
Journal code: 9421292. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB In Great Britain an independent scientific review for the government has concluded that the development of a cattle vaccine against Mycobacterium bovis infection holds the best long-term prospect for tuberculosis control in British herds. A precondition for vaccination is the development of a complementary diagnostic test to differentiate between vaccinated animals and those infected with M. bovis so that testing and slaughter-based control strategies can continue alongside vaccination. To date bacillus Calmette-Guerin (BCG), an attenuated strain of M. bovis, is the only available vaccine for the prevention of tuberculosis. However, tests based on tuberculin purified protein derivative cannot distinguish between M. bovis infection and BCG vaccination. Therefore, specific antigens expressed by M. bovis but absent from BCG constitute prime candidates for differential diagnostic reagents. Recently, two such antigens, ESAT-6 and CFP-10, have been reported to be promising candidates as diagnostic

reagents for the detection of M. bovis infection in cattle. Here we report the identification of promiscuous peptides of CFP-10 that were recognized by M. bovis-infected cattle. Five of these peptides were formulated into a peptide cocktail together with five peptides derived from ESAT-6. Using this peptide cocktail in **T-cell** assays, M. bovis-infected animals were detected, while BCG-vaccinated or Mycobacterium avium-sensitized animals did not respond. The sensitivity of the peptide cocktail as an antigen in a whole-blood gamma interferon assay was determined using naturally infected field reactor cattle, and the specificity was determined using blood from BCG-vaccinated and noninfected, nonvaccinated animals. The sensitivity of the assay in cattle with confirmed tuberculosis was found to be 77.9%, with a specificity of 100% in BCG-vaccinated or nonvaccinated animals. This compares favorably with the specificity of tuberculin when tested in noninfected or vaccinated animals. In summary, our results demonstrate that this peptide cocktail can discriminate between M. bovis infection and BCG vaccination with a high degree of sensitivity and specificity.

L80 ANSWER 3 OF 62 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000278113 MEDLINE
DOCUMENT NUMBER: 20278113 PubMed ID: 10816479
TITLE: Antigenic equivalence of human **T-cell** responses to Mycobacterium tuberculosis-specific RD1-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides.
AUTHOR: Arend S M; Geluk A; van Meijgaarden K E; van Dissel J T; Theisen M; Andersen P; Ottenhoff T H
CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands.. smarend@lumc.nl
SOURCE: INFECTION AND IMMUNITY, (2000 Jun) 68 (6) 3314-21. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706
Entered Medline: 20000623

AB The early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of tuberculosis. Both antigens are encoded by RD1, a genomic region present in all strains of Mycobacterium tuberculosis and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Production and purification of recombinant antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 (rCFP-10) can be replaced with corresponding mixtures of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. tuberculosis-specific human **T-cell** lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixtures were almost completely correlated ($r = 0.96$, $P < 0.0001$ for ESAT-6; $r = 0.98$, $P < 0.0001$ for CFP-10). More importantly, the same was found when gamma interferon production by peripheral blood mononuclear cells in response to these stimuli was analyzed ($r = 0.89$, $P < 0.0001$ for ESAT-6; $r = 0.89$, $P < 0.0001$ for CFP-10). Whole protein antigens and the peptide mixtures resulted in identical sensitivity and specificity for detection of infection with M. tuberculosis. The peptides in each mixture contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were

significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixtures of synthetic overlapping peptides have potency equivalent to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. tuberculosis, and peptides have the advantage of faster production at lower cost.

L80 ANSWER 4 OF 62 MEDLINE on STN
ACCESSION NUMBER: 2002271820 MEDLINE
DOCUMENT NUMBER: 22006907 PubMed ID: 12010994
TITLE: Correlation of ESAT-6-specific gamma interferon production with pathology in cattle following Mycobacterium bovis BCG vaccination against experimental bovine tuberculosis.
AUTHOR: Vordermeier H Martin; Chambers Mark A; Cockle Paul J; Whelan Adam O; Simmons Jennifer; Hewinson R Glyn
CORPORATE SOURCE: Veterinary Laboratories Agency Weybridge, TB Research Group, New Haw, Addlestone, Surrey KT15 3NB, United Kingdom.. mvordermeier.vla@gtnet.gov.uk
SOURCE: INFECTION AND IMMUNITY, (2002 Jun) 70 (6) 3026-32. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020516
Last Updated on STN: 20020627
Entered Medline: 20020626

AB Vaccine development and the understanding of the pathology of bovine tuberculosis in cattle would be greatly facilitated by the definition of immunological correlates of protection and/or pathology. To address these questions, cattle were vaccinated with Mycobacterium bovis bacillus Calmette-Guerin (BCG) and were then challenged with virulent M. bovis. Applying a semiquantitative pathology-scoring system, we were able to demonstrate that BCG vaccination imparted significant protection by reducing the disease severity on average by 75%. Analysis of cellular immune responses following M. bovis challenge demonstrated that proliferative **T-cell** and gamma interferon (IFN-gamma) responses towards the M. bovis-specific antigen ESAT-6, whose gene is absent from BCG, were generally low in vaccinated animals but were high in all nonvaccinated calves. Importantly, the amount of ESAT-6-specific IFN-gamma measured by enzyme-linked immunosorbent assay after M. bovis challenge, but not the frequency of responding cells, correlated positively with the degree of pathology found 18 weeks after infection. Diagnostic reagents based on antigens not present in BCG, like ESAT-6 and CFP-10, were still able to distinguish BCG-vaccinated, diseased animals from BCG-vaccinated animals without signs of disease. In summary, our results suggest that the determination of ESAT-6-specific IFN-gamma, while not a direct correlate of protection, constitutes nevertheless a useful prognostic immunological marker predicting both vaccine efficacy and disease severity.

L80 ANSWER 5 OF 62 MEDLINE on STN
ACCESSION NUMBER: 2002024114 MEDLINE
DOCUMENT NUMBER: 21360002 PubMed ID: 11467375
TITLE: Uncommon presentations of tuberculosis: the potential value of a novel diagnostic assay based on the Mycobacterium tuberculosis-specific antigens ESAT-6 and CFP-10.
AUTHOR: Arend S M; Ottenhoff T H; Andersen P; van Dissel J T
CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, The Netherlands.. s.m.arend@lumc.nl
SOURCE: INTERNATIONAL JOURNAL OF TUBERCULOSIS AND LUNG DISEASE,

(2001 Jul) 5 (7) 680-6.
Journal code: 9706389. ISSN: 1027-3719.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011205

AB SETTING: Leiden University Medical Center, Leiden, the Netherlands. OBJECTIVE: To illustrate the potential value of a recently developed diagnostic assay for detection of tuberculosis (TB), based on **T cell** responses to the early secreted antigenic target 6 kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10). These antigens are Mycobacterium tuberculosis specific because they are expressed by M. tuberculosis but absent from M. bovis bacille Calmette-Guerin (BCG) and most environmental mycobacteria. In recent studies, the assay had a high sensitivity and specificity for detection of active TB. DESIGN: We describe five patients with uncommon presentations of tuberculosis, in whom the diagnosis was delayed by negative or conflicting results of diagnostic procedures aimed at detection of M. tuberculosis and an uninformative tuberculin skin test. IFN-gamma production in response to ESAT-6 and CFP-10 by peripheral blood mononuclear cells from these patients was evaluated before and during anti-tuberculosis treatment. RESULTS: In all five patients, IFN-gamma responses to ESAT-6 and/or CFP-10 were above the cut-off level defined in a previous study. During treatment, IFN-gamma responses generally increased. CONCLUSION: These results indicate that **T cell** responses to M. tuberculosis-specific antigens have potential diagnostic value when TB is suspected and the results of other diagnostic tests are inconclusive, especially in BCG-vaccinated individuals.

L80 ANSWER 6 OF 62 MEDLINE on STN
ACCESSION NUMBER: 2001414824 MEDLINE
DOCUMENT NUMBER: 21357299 PubMed ID: 11463236
TITLE: BOVIGAM: an in vitro cellular diagnostic test for bovine tuberculosis.
AUTHOR: Wood P R; Jones S L
CORPORATE SOURCE: Research and Development, CSL Animal Health, 45 Poplar Road, Parkville, Victoria, Australia.. paul-wood@csl.com.au
SOURCE: Tuberculosis (Edinb), (2001) 81 (1-2) 147-55. Ref: 139
Journal code: 100971555. ISSN: 1472-9792.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20021030
Entered Medline: 20010906

AB BOVIGAM which is based on the detection of gamma interferon (IFN- gamma) is a rapid, laboratory assay of a cell mediated immune response that may be used for the detection of tuberculosis (TB) infection in animals. Whole blood is first incubated overnight with bovine PPD, avian PPD or negative control antigens, and IFN- gamma in the supernatant plasma is then measured by EIA. TB infection is indicated by a predominant IFN-gamma response to bovine PPD. Since 1988, BOVIGAM has been extensively trialed on more than 200 000 cattle in Australia, Brazil, Ireland,

Northern Ireland, Italy, New Zealand, Romania, Spain and the USA. Sensitivity has varied between 81.8% and 100% for culture-confirmed bovine TB and specificity between 94% and 100%. The IFN- gamma assay detects M. bovis infection earlier than the skin test and in New Zealand is applied to detect skin-test negative cattle with TB, where after slaughter a significant number of IFN- gamma reactors have TB. BOVIGAM is also approved in New Zealand for serial testing skin test positive cattle when non-specificity is suspected. Cattle are tested 7-30 days after a positive caudal fold test. The boosting effect of the skin test on **T-cell** activity allows blood to be cultured with PPD up to 30 h after collection without effecting accuracy.The BOVIGAM results are not affected by poor nutritional condition and are only mildly and briefly affected by dexamethasone treatment and parturition. IFN- gamma responses of cattle vaccinated with BCG are dose-dependent and short-lived. The BOVIGAM kit is now used routinely in many countries for the detection of M. bovis infected cattle, buffalo and goats.

L80 ANSWER 7 OF 62 MEDLINE on STN
ACCESSION NUMBER: 2001414818 MEDLINE
DOCUMENT NUMBER: 21357293 PubMed ID: 11463230
TITLE: Immune responses in bovine tuberculosis.
AUTHOR: Pollock J M; McNair J; Welsh M D; Girvin R M; Kennedy H E; Mackie D P; Neill S D
CORPORATE SOURCE: Veterinary Sciences Division, Department of Agriculture and Rural Development, Stoney Road, Stormont, Belfast, BT4 3SD, UK.
SOURCE: Tuberculosis (Edinb), (2001) 81 (1-2) 103-7. Ref: 49
Journal code: 100971555. ISSN: 1472-9792.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20021030
Entered Medline: 20010906

AB Knowledge of the immune responses which develop in cattle following infection with Mycobacterium bovis is essential both to the understanding of disease pathogenesis and to the logical development of immune-dependent tools, such as diagnostic tests and vaccines, which can be used to combat the disease. Studies of field cases of bovine tuberculosis (TB) and of experimental bovine models of M. bovis infection have indicated that cell-mediated immune responses (CMI) predominate within a spectrum of immunity which exists. This paper reviews aspects of recent research and indicates how knowledge of **T-cell** antigenic targets in bovine TB along with increasing knowledge of **T-cell** subpopulations and their interactions with M. bovis -infected macrophages provides opportunities for the development of better methods for disease control.

L80 ANSWER 8 OF 62 MEDLINE on STN
ACCESSION NUMBER: 2001233254 MEDLINE
DOCUMENT NUMBER: 21111927 PubMed ID: 11174139
TITLE: Erythema induratum in a patient with active tuberculosis of the axillary lymph node: IFN-gamma release of specific **T cells**.
AUTHOR: Koga T; Kubota Y; Kiryu H; Nakayama J; Matsuzoe D;

Shirakusa T
CORPORATE SOURCE: Department of Dermatology, School of Medicine, Fukuoka University, 3-1-1, Maidashi, Higashi-ku, J-812-8582 Fukuoka, Japan.. tekoga@dermatol.med.kyushu-u.ac.jp
SOURCE: EUROPEAN JOURNAL OF DERMATOLOGY, (2001 Jan-Feb) 11 (1) 48-9.
Journal code: 9206420. ISSN: 1167-1122.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010503

AB A 57-year-old woman with tender nodular lesions on her legs, arms, buttocks and face is reported as a case of erythema induratum (EI) with active tuberculosis of axillary lymph nodes. Both skin nodular lesions and lymph nodes responded positively to antituberculous therapy. The patient's peripheral blood mononuclear cells showed a high proliferation and produced interferon-gamma (IFN-gamma) in response to purified protein derivative (PPD). These findings indicate the possibility that PPD-specific **T cells**, capable of producing IFN-gamma, are likely to be involved in the formation of EI as a type of delayed-type hypersensitivity response to mycobacterial antigens at the site of skin lesions.

L80 ANSWER 9 OF 62 MEDLINE on STN
ACCESSION NUMBER: 2000417694 MEDLINE
DOCUMENT NUMBER: 20336500 PubMed ID: 10875803
TITLE: Toward the development of diagnostic assays to discriminate between Mycobacterium bovis infection and bacille Calmette-Guerin vaccination in cattle.
AUTHOR: Vordermeier H M; Cockle P J; Whelan A O; Rhodes S; Hewinson R G
CORPORATE SOURCE: Tuberculosis Research Group, Bacteriology Department, Veterinary Laboratories Agency-Weybridge, New Haw, Addlestone, Surrey KT15 3NB, United Kingdom.. mvordermeier.vla@gtnet.gov.uk
SOURCE: CLINICAL INFECTIOUS DISEASES, (2000 Jun) 30 Suppl 3 S291-8.
Journal code: 9203213. ISSN: 1058-4838.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000906

AB A scientific review of the recent sharp increase in bovine tuberculosis in Great Britain has concluded that the development of a cattle vaccine holds the best prospect for long-term disease control. It is important to develop a diagnostic test that differentiates between vaccinated and Mycobacterium bovis-infected animals, to ensure that test-and-slaughter control strategies can continue alongside vaccination. The mycobacterial antigens ESAT-6, MPB64, and MPB83 are expressed at high levels in M. bovis but are expressed at low levels or not at all in bacille Calmette-Guerin (BCG) Pasteur. Promiscuous bovine **T cell** epitopes of these antigens were identified and formulated into a peptide cocktail. This cocktail and a cocktail composed of recombinant forms of the 3 antigens was able to distinguish cattle infected with virulent M. bovis

from those vaccinated with BCG and from those sensitized to avian tuberculin in lymphocyte transformation and interferon-gamma assays.

L80 ANSWER 10 OF 62 MEDLINE on STN
ACCESSION NUMBER: 1999403264 MEDLINE
DOCUMENT NUMBER: 99403264 PubMed ID: 10473516
TITLE: Development of diagnostic reagents to differentiate between Mycobacterium bovis BCG vaccination and M. bovis infection in cattle.
AUTHOR: Vordermeier H M; Cockle P C; Whelan A; Rhodes S; Palmer N; Bakker D; Hewinson R G
CORPORATE SOURCE: TB Research Group, Bacteriology Department, Veterinary Laboratories Agency-Weybridge, New Haw, Addlestone, KT15 3NB, United Kingdom.. mvordermeier.vla@gtnet.gov
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (1999 Sep) 6 (5) 675-82.
Journal code: 9421292. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991027

AB In Great Britain a recent independent scientific review for the government has concluded that the development of a cattle vaccine against Mycobacterium bovis holds the best long-term prospect for tuberculosis control in British herds. A sine qua non for vaccination is the development of a complementary diagnostic test to differentiate between vaccinated animals and those infected with M. bovis so that test-and-slaughter-based control strategies can continue alongside vaccination. In order to assess the feasibility of developing a differential diagnostic test for a live vaccine, we chose M. bovis BCG Pasteur as a model system. Recombinant forms of antigens which are expressed in M. bovis but not, or only at low levels, in BCG Pasteur (ESAT-6, MPB64, MPB70, and MPB83) were produced. These reagents were tested either alone or in combination by using peripheral blood mononuclear cells from M. bovis-infected, BCG-vaccinated, and Mycobacterium avium-sensitized calves. All four antigens induced in vitro proliferation and gamma interferon responses only in M. bovis-infected animals. A cocktail composed of ESAT-6, MPB64, and MPB83 identified infected animals but not those vaccinated with BCG. In addition, promiscuous **T-cell** epitopes of ESAT-6, MPB64, and MPB83 were formulated into a peptide cocktail. In **T-cell** assays with this peptide cocktail, infected animals were identified with frequencies similar to those obtained in assays with the protein cocktail, while BCG-vaccinated or M. avium-sensitized animals did not respond. In summary, our results suggest that peptide and protein cocktails can be designed to discriminate between M. bovis infection and BCG vaccination.

L80 ANSWER 11 OF 62 MEDLINE on STN
ACCESSION NUMBER: 1998304422 MEDLINE
DOCUMENT NUMBER: 98304422 PubMed ID: 9640240
TITLE: Recognition of a common mycobacterial **T-cell** epitope in MPB59 of Mycobacterium bovis.
AUTHOR: Lightbody K A; Girvin R M; Pollock D A; Mackie D P; Neill S D; Pollock J M
CORPORATE SOURCE: Department of Veterinary Sciences, Queen's University of Belfast, UK.

SOURCE: IMMUNOLOGY, (1998 Mar) 93 (3) 314-22.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980707

AB Bovine tuberculosis, which persists as a residual level of infection in many European countries, has implications not only for the economy of farming communities but also for human health. The aim of this study was to identify a common mycobacterial antigen which was recognized in bovine tuberculosis and to characterize the response to this antigen at the epitope level. A **T-cell** clone, phenotype CD4+, raised from an animal experimentally infected with Mycobacterium bovis was shown to proliferate in response to a panel of sonicates derived from different mycobacterial species indicating recognition of an antigen with broad specificity. This antigen was subsequently shown to be MPB59. Recognition of MPB59 at the epitope level was determined in experimental and field cases of bovine tuberculosis using a panel of synthetic peptides (20-mers with 10-residue overlaps) incorporating the signal sequence and mature protein. The results showed that in vitro interferon-gamma was predominantly produced in response to adjacent peptides numbers 10 and 11, suggesting that the dominant epitope was contained in the overlap, correlating to residues 101-110 (YYQSGLSIVM). This epitope was recognized by 54% of tuberculous cattle of mixed breeds, which suggests that it may be genetically permissive in terms of major histocompatibility complex presentation. Sequence analysis confirmed that there were only minor differences in the amino acid composition within this region for various mycobacterial species, which could explain the common **T-cell** recognition described in this study. Common recognition of this epitope indicates that it would have limited potential for use as a diagnostic reagent per se but may have potential for inclusion in a subunit vaccine.

L80 ANSWER 12 OF 62 MEDLINE on STN
ACCESSION NUMBER: 97193802 MEDLINE
DOCUMENT NUMBER: 97193802 PubMed ID: 9041387
TITLE: Evaluation of the recombinant 38-kilodalton antigen of Mycobacterium tuberculosis as a potential immunodiagnostic reagent.
AUTHOR: Wilkinson R J; Haslov K; Rappuoli R; Giovannoni F; Narayanan P R; Desai C R; Vordermeier H M; Paulsen J; Pasvol G; Ivanyi J; Singh M
CORPORATE SOURCE: MRC Tuberculosis and Related Infections Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London, United Kingdom.
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1997 Mar) 35 (3) 553-7.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602

AB The diagnosis of infection caused by Mycobacterium tuberculosis is of increased public health concern following increases in the number of cases

in developed countries and major increases in developing countries associated with the spread of human immunodeficiency virus (HIV) infection. The specificity of purified protein derivative skin testing for the detection of infection is compromised by exposure to environmental mycobacteria. Examination of sputum detects the most infectious patients, but not those with extrapulmonary disease. The 38-kDa antigen of M. tuberculosis contains two M. tuberculosis-specific B-cell epitopes. We overexpressed the gene for this antigen in Escherichia coli and evaluated the recombinant product in in vitro assays of **T-cell** function and as a target for the antibody response in humans. The sensitivity and specificity of the antigen as a skin test reagent were also assessed in outbred guinea pigs. We found that 69% of healthy sensitized humans recognize the antigen in vitro, as manifested by both cell proliferation and the production of gamma interferon. Untreated patients initially have a lower frequency of response (38%); this recovers to 72% during therapy. A total of 292 patients (20 with HIV coinfection) and 58 controls were examined for production of antibody to the 38-kDa antigen by using a commercially available kit. The sensitivity of the test in comparison with that of culture was 72.6%, and the specificity was 94.9%. The antigen was also tested for its ability to induce skin reactions in outbred guinea pigs sensitized by various mycobacterial species. The antigen provoked significant skin reactions in M. tuberculosis-, M. bovis BCG-, and M. intracellulare-sensitized animals. The significance of these findings and the usefulness of this antigen in immunodiagnosis are discussed.

L80 ANSWER 13 OF 62 MEDLINE on STN
ACCESSION NUMBER: 1998438964 MEDLINE
DOCUMENT NUMBER: 98438964 PubMed ID: 9765827
TITLE: Glycolipid antigen for use in diagnostic assays for bovine tuberculosis.
AUTHOR: Ostyn A; Laneelle M A; Thorel M F
CORPORATE SOURCE: CNEVA Alfort, Maisons-Alfort, France.
SOURCE: RESEARCH IN MICROBIOLOGY, (1997 Jul-Aug) 148 (6) 491-500. Journal code: 8907468. ISSN: 0923-2508.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981102

AB A glycolipid antigen, was isolated, purified and characterized from Mycobacterium bovis An5. Chemical analysis (thin-layer chromatography, nuclear magnetic resonance and infrared spectra) showed that this glycolipid was a 2,3-di-O-acyl trehalose (DAT), similar to the DAT of M. tuberculosis. This antigen was used to establish ELISA-based serodiagnostic tests for M. bovis-infected cattle. The sensitivity and specificity of the assay were investigated using sera of cattle from tuberculosis-free herds and from tuberculosis-infected herds. No correlation was found between DAT-ELISA and the skin test, nor between DAT-ELISA and interferon-gamma with bovine purified protein derivative. The antibody titres were not related to cell-mediated immunity. Although the antigen was highly specific (95.9%), the sensitivity of DAT-ELISA, as judged from assays in bacteriologically confirmed tuberculosis, was low (29 to 36.8%). The low sensitivity of ELISA might also be attributed to a reciprocal relationship between B-cell proliferation and **T-cell** protective immunity.

L80 ANSWER 14 OF 62 MEDLINE on STN

ACCESSION NUMBER: 94353623 MEDLINE
DOCUMENT NUMBER: 94353623 PubMed ID: 8073620
TITLE: In vitro immunodiagnostic assays for bovine tuberculosis.
AUTHOR: Wood P R; Rothel J S
CORPORATE SOURCE: CSIRO, Division of Animal Health, Parkville, Vic, Australia.
SOURCE: VETERINARY MICROBIOLOGY, (1994 May) 40 (1-2) 125-35. Ref: 51
Journal code: 7705469. ISSN: 0378-1135.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941006
Last Updated on STN: 19941006
Entered Medline: 19940929

AB The immune response to mycobacterial infections in cattle is predominantly cellular in nature and current diagnostic tests for M. bovis are based on the measurement of **T cell** responses. The low sensitivity of serological assays for tuberculosis is therefore not surprising and serological tests will at best be used to complement rather than replace cellular assays. The recently developed bovine interferon gamma (IFN-gamma) assay is a rapid (24 hour) and simple whole blood in vitro assay, which in Australian field trials was found to be significantly more sensitive than the intradermal tuberculin test for the diagnosis of bovine tuberculosis. The problem of false-positive reactions, due to the cross-reactive nature of the antigen preparations used, can largely be overcome by using a comparative assay in which an animal's IFN-gamma response to bovine PPD and avian PPD are compared. Although reasonably M. bovis specific proteins have been identified and characterised, their use in either serological or cellular diagnostic assays is likely to be restricted due to the genetic diversity of the bovine immune response to M. bovis infection.

L80 ANSWER 15 OF 62 MEDLINE on STN
ACCESSION NUMBER: 94321007 MEDLINE
DOCUMENT NUMBER: 94321007 PubMed ID: 7519175
TITLE: Identification of bovine **T-cell** epitopes for three Mycobacterium bovis antigens: MPB70, 19,000 MW and MPB57.
AUTHOR: Pollock J M; Douglas A J; Mackie D P; Neill S D
CORPORATE SOURCE: Department of Agriculture for Northern Ireland, Veterinary Sciences Division, Stormont, Belfast.
SOURCE: IMMUNOLOGY, (1994 May) 82 (1) 9-15.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940909
Last Updated on STN: 19960129
Entered Medline: 19940831

AB Bovine tuberculosis remains a serious problem in several regions, partly due to a lack of specific diagnostic tests. The aim of this study was to identify bovine **T-cell** epitopes for defined Mycobacterium bovis antigens using an experimental model of the natural disease. Panels of synthetic peptides (16-mers with five residue

overlaps) were produced from published amino acid sequences for MPB70, the 19,000 MW antigen and MPB57. In vitro lymphocyte proliferation assays were used to identify **T-cell** epitopes. Lymphocytes from experimentally infected cattle proliferated in response to five epitopes (residues 88-105 and 144-163 for MPB70; 1-16 and 67-84 for the 19,000 MW antigen; and 85-100 for MBP57). These epitopes were not recognized by control, non-infected animals, but were recognized by field reactors to intradermal tuberculin testing. All five epitopes were recognized by three different breeds of cattle (Friesian, Charolais and Simmental). In addition, the bovine **T-cell** epitopes identified for the 19,000 MW antigen in this study were similar to epitopes previously reported for man and mouse. Thus, as well as identifying candidate reagents for improved diagnostic tests and vaccination, this study provides evidence for genetic promiscuity **T-cell** recognition of major myobacterial epitopes.

L80 ANSWER 16 OF 62 CAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 1
ACCESSION NUMBER: 2002:520032 CAPLUS
DOCUMENT NUMBER: 137:277445
TITLE: Enhancement of human T cell response to a peptide epitope of 38 kDa antigen of Mycobacterium tuberculosis by liposomes
AUTHOR(S): Bala, Lakshmi; Anand, Sukumar; Sinha, Sudhir
CORPORATE SOURCE: Division of Biochemistry, Central Drug Research Institute, Lucknow, India
SOURCE: Immunopharmacology and Immunotoxicology (2002), 24(2), 255-263
CODEN: IITOEF; ISSN: 0892-3973
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Diagnosis of tuberculosis is a problem, specially in the regions harboring an abundance of both pathogenic and non- pathogenic mycobacteria. This study was undertaken to assess in such a situation the predictive value of proliferative T cell response to a peptide epitope ("38G") of the 38 kDa membrane protein of Mycobacterium tuberculosis. 3[H]thymidine incorporation assays were done with peripheral blood mononuclear cells of tuberculoid leprosy and pulmonary tuberculosis patients. The donors were also classified as PPD responders (Stimulation Index, SI > 3) or non-responders (SI .ltoreq. 3) on the basis of their T cell response to the "Purified Protein Deriv. (PPD)" of M. tuberculosis. 38G peptide was used in either free or liposome-assocd. form. While free peptide failed to induce a pos. response in study subjects, its liposomal form was T cell stimulatory and distinguished, to certain extent, between PPD responders (corresponding SI > 3 in 54% subjects) and non-responders (SI > 3 in 29% subjects). However, it did not differentiate between leprosy and tuberculosis. The study supports use of liposomes as adjuvant vehicles for antigenic peptides designed to activate human T cells.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 17 OF 62 CAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 4
ACCESSION NUMBER: 2000:790341 CAPLUS
DOCUMENT NUMBER: 133:349130
TITLE: **Proteins** expressed by Mycobacterium tuberculosis and not by BCG and their use as diagnostic reagents and vaccines
INVENTOR(S): Gennaro, Maria L.
PATENT ASSIGNEE(S): The Public Health Research Institute of the City of New York, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066157	A1	20001109	WO 2000-US12257	20000504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1214088	A1	20020619	EP 2000-928851	20000504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003519467	T2	20030624	JP 2000-615041	20000504

PRIORITY APPLN. INFO.: US 1999-132505P A1 19990504
WO 2000-US12257 W 20000504

AB The invention provides polypeptides encoded by open reading frames present in the genome of Mycobacterium tuberculosis but absent from the genome of BCG and diagnostic and prophylactic methodologies using these polypeptides. The disclosed polypeptides are MTBN1-8, i.e. Mycobacterium tuberculosis BCG-neg. protein or antigen 1-8.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 18 OF 62 CAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 6
ACCESSION NUMBER: 2000:469625 CAPLUS
DOCUMENT NUMBER: 134:146084
TITLE: IgG isotype antibody responses to epitopes of the Mycobacterium bovis protein MPB70 in immunized and in tuberculin skin test-reactor cattle
AUTHOR(S): Lightbody, K. A.; McNair, J.; Neill, S. D.; Pollock, J. M.
CORPORATE SOURCE: Department of Veterinary Sciences, Queen's University of Belfast, Belfast, BT7 1NN, Ire.
SOURCE: Veterinary Microbiology (2000), 75(2), 177-188
CODEN: VMICDQ; ISSN: 0378-1135
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serol. assays may have merit in identifying animals in advanced stages of bovine tuberculosis, but most tests have had sub-optimal sensitivities and specificities. The Mycobacterium bovis protein MPB70 has been identified as a B-cell target with diagnostic potential in measurement of pre- and post-skin-test antibody responses. One observation, which has potential practical application, has been that skin testing with tuberculin boosts IgG1 anti-MPB70 antibody responses in cattle with tuberculous lesions. However, serol. cross-reactivities with bacteria, such as Nocardia asteroides, have been described for this protein. With the aim of identifying candidate reagents for improved diagnostic tests, this study investigated IgG isotype antibody responses to MPB70 at the epitope level and, because of the previous findings, focused on IgG1 responses following skin testing. Screening of a panel of overlapping synthetic peptides using sera from cattle immunized with MPB70 and cattle infected with M.

bovis showed that two regions of the protein (residues 21-70 and 101-120) contain dominant B-cell epitopes. No individual epitope appeared to be selectively recognized by one isotype of IgG antibody. Investigation of IgG1 responses showed that recognition of the epitope within residues 51-70 was boosted strongly by tuberculin injections in skin-test pos. cattle and that this memory response was generally a feature of cattle which were found to have macroscopic, tuberculous lesions.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 19 OF 62 CAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 7
ACCESSION NUMBER: 1993:404422 CAPLUS
DOCUMENT NUMBER: 119:4422
TITLE: Diagnostic peptides derived from Mycobacterium tuberculosis antigens
INVENTOR(S): Vordermeier, Hans; Harris, David; Moreno, Carlos; Ivanyi, Juraj
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9221697	A2	19921210	WO 1992-GB948	19920526
WO 9221697	A3	19930513		
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9217616	A1	19930108	AU 1992-17616	19920526
AU 667305	B2	19960321		
EP 586465	A1	19940316	EP 1992-910821	19920526
R: DE, DK, FR, GB, IT, NL				

PRIORITY APPLN. INFO.: GB 1991-11291 19910524
WO 1992-GB948 19920526

AB Tuberculosis is diagnosed in humans or animals by use of a peptide derived from the 38-kDa lipoprotein antigen of M. tuberculosis in place of PPD in a skin delayed hypersensitivity test or a lymphocyte activation test. These tests can distinguish between patients with active tuberculosis and sensitized individuals, and is thus more specific than tests using PPD. The peptide comprises residues 350-369 (or 353-362) of the lipoprotein or variants or immunol. equivs. thereof. Peptides corresponding to residues 45-64 and 61-80 of a 19-kDa protein of M. tuberculosis can be used similarly. Thus, the lymphocyte proliferative response was strong with synthetic peptides 350-369, 1-20, 65-83, and 325-342 of the 38-kDa lipoprotein for most PPD-pos. healthy subjects and lymphatic tuberculosis patients, and absent for PPD-neg. healthy subjects; the response was neg. for peptide 350-369 in 89% of patients with pulmonary tuberculosis and 75% of patients with nonlymphatic extrapulmonary tuberculosis, whereas the response was pos. with the other 3 peptides in these patients.

L80 ANSWER 20 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:118086 CAPLUS
DOCUMENT NUMBER: 138:168794
TITLE: Early detection of mycobacterial disease using peptides
INVENTOR(S): Laal, Suman; Zolla-Pazner, Susan; Belisle, John T.

PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003012395	A2	20030213	WO 2002-US24297	20020802

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-309185P P 20010802

AB A no. of protein and glycoprotein antigens secreted by Mycobacterium tuberculosis (Mtb) have been identified as "early" Mtb antigens on the basis of early antibodies present in subjects infected with Mtb prior to the development of detectable clin. disease. Epitope-bearing peptide fragments of these early Mtb antigens, in particular of an 88 kDa secreted protein, GlcB (SEQ ID NO:106) and of Mtb antigen MPT51 (SEQ ID NO:107) have been identified. These peptides, variants thereof, peptide multimers thereof that include two or more repeats of one or more of the peptides, and fusion polypeptides that include early Mtb antigenic proteins, peptides or both, are useful in immunoassay methods for early, rapid detection of TB in a subject. Preferred immunoassays detect the antibodies in the subject's urine. Also provided are antigenic compns., kits and methods useful for detecting early Mtb antibodies. The antigenic proteins and peptides are also used in vaccine compns.

L80 ANSWER 21 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:454921 CAPLUS
DOCUMENT NUMBER: 139:26662
TITLE: Compositions and methods for the prevention, treatment and detection of tuberculosis and other diseases
INVENTOR(S): Leishman, Kathryn
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 18,243, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003108927	A1	20030612	US 2002-265190	20021007
WO 2000078342	A1	20001228	WO 2000-US16679	20000619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-194766P P 20000403
US 2000-206518P P 20000522
WO 2000-US16679 W 20000619
US 2000-18243 B2 20011218
US 1999-335891 A2 19990618

AB Methods and compns. are provided for the prevention and treatment of infectious diseases such as syphilis, tuberculosis, pneumonia, other bacterial infections, AIDS, and other viral infections. Many of the compns. are active against carbon monoxide dehydrogenase (CODH), and include substances such as antigens, antibodies specific for CODH, and other inhibitors of CODH such as nickel and molybdenum metal chelators. The methods and compns. are particularly suited for treatment of diseases from previously under-recognized anaerobic or facultative anaerobic pathogens such as Mycobacterium tuberculosis and Mycobacterium pneumoniae.

L80 ANSWER 22 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:466033 CAPLUS
DOCUMENT NUMBER: 137:28273
TITLE: MHC class I associated peptides for prevention and treatment of tuberculosis
INVENTOR(S): Flyer, David; Ross, Mark M.; Hunt, Donald F.; White, Forest M.
PATENT ASSIGNEE(S): Argonex Pharmaceuticals, USA; University of Virginia Patent Foundation
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002048175	A2	20020620	WO 2001-US48742	20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002027406	A5	20020624	AU 2002-27406	20011212
US 2002192229	A1	20021219	US 2001-22286	20011213

PRIORITY APPLN. INFO.: US 2000-255292P P 20001213
US 2001-264978P P 20010130
WO 2001-US48742 W 20011212

AB The present invention relates to compns. and methods for the prevention, treatment, and diagnosis of tuberculosis, and discloses peptides, polypeptides, and polynucleotides that can be used to stimulate a CTL response against tuberculosis. The peptide and/or proteins of the invention may be used as a therapeutic drug to stimulate the immune system to recognize and eliminate Mycobacterium tuberculosis in infected cells or as a vaccine for the prevention of disease. Antibodies that react with the immunogens of the invention, as well as methods of using these

antibodies for prevention and treatment of disease, are also disclosed.

L80 ANSWER 23 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:450573 CAPLUS
DOCUMENT NUMBER: 137:293192
TITLE: Human T cell responses to peptides of the Mycobacterium leprae 45-kD serine-rich antigen
AUTHOR(S): Brahmbhatt, S.; Hussain, R.; Zafar, S.; Dawood, G.; Ottenhoff, T. H. M.; Drijfhout, J. W.; Bothamley, G.; Smith, S.; Lopez, F. V.; Dockrell, H. M.
CORPORATE SOURCE: Immunology Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, WC1E 7HT, UK
SOURCE: Clinical and Experimental Immunology (2002), 128(1), 140-148
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to identify T cell epitopes within the Mycobacterium leprae 45 kDa serine-rich antigen, we analyzed responses to overlapping 17-mer peptides encompassing the whole antigen in non-exposed UK controls, Pakistani leprosy patients and tuberculosis patients in both the United Kingdom and Pakistan. This antigen has been described as M. leprae-specific, although it has a hypothetical homolog in M. tuberculosis. Human peripheral blood mononuclear cells were stimulated with peptide for 5 days and IFN-.gamma. measured in supernatants by ELISA. Some peptides were recognized more frequently by T cells from tuberculoid leprosy patients than those from UK controls, suggesting that such T cell epitopes might have diagnostic potential, while other peptides induced greater responses among UK control subjects. Short-term cell lines confirmed that these assays detected specific T cell recognition of these peptides. However, many tuberculosis patients also recognized these potentially specific peptides suggesting that there could be a true homolog present in M. tuberculosis.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 24 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:780953 CAPLUS
DOCUMENT NUMBER: 135:343273
TITLE: Cloning and immunogenicity of Mycobacterium tuberculosis proteins
INVENTOR(S): Agger, Else Marie; Andersen, Peter; Okkels, Li Mei Meng; Weldingh, Karin
PATENT ASSIGNEE(S): Statens Serum Institut, Den.
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079274	A2	20011025	WO 2001-DK276	20010419
WO 2001079274	A3	20020711		
WO 2001079274	B1	20020808		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1278769 A2 20030129 EP 2001-923542 20010419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: DK 2000-666 A 20000419
DK 2001-283 A 20010221
WO 2001-DK276 W 20010419

AB The authors disclose the identification and characterization of a no. of novel Mycobacterium tuberculosis derived proteins and protein fragments. The proteins and protein fragments were examd. for their ability to elicit interferon-.gamma. prodn. and/or a T-cell proliferative response in guinea pigs and humans with tuberculosis.

L80 ANSWER 25 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:861717 CAPLUS
DOCUMENT NUMBER: 134:16511
TITLE: Immunodiagnosis of tuberculosis and other mycobacterial infections
INVENTOR(S): Haak-Frendscho, Mary; Landowski, Christopher; Lesley, Scott
PATENT ASSIGNEE(S): Promega Corporation, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073345	A2	20001207	WO 2000-US14546	20000526
WO 2000073345	A3	20010525		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1999-322202 A 19990528

AB The authors disclose the prepn. and reactivity of antibodies specific for peptides of mycobacterial antigens. In one example, chickens were immunized with fusion proteins contg. peptides derived from Ag85, 14-kDa, and 38-kDa antigens of Mycobacterium tuberculosis. The antibodies demonstrated utility in serodiagnosis of tuberculosis.

L80 ANSWER 26 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:790327 CAPLUS
DOCUMENT NUMBER: 133:332032
TITLE: Secreted proteins of Mycobacterium tuberculosis and their use in vaccines and diagnostic reagents
INVENTOR(S): Gennaro, Maria L.; Gomez, Manuel J.
PATENT ASSIGNEE(S): The Public Health Research Institute of the City of

New York, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066143	A1	20001109	WO 2000-US12197	20000504

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-132479P P 19990504
US 1999-132503P P 19990504

AB The invention provides Mycobacterium tuberculosis polypeptides and genes encoding them for use in diagnostic and prophylactic methodologies. The proteins were identified in sequence databases by querying them for signal peptide-like sequences.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 27 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:685472 CAPLUS
DOCUMENT NUMBER: 133:333674
TITLE: Increased numbers of ESAT-6- and purified protein derivative-specific gamma interferon-producing cells in subclinical and active tuberculosis infection
AUTHOR(S): Ulrichs, Timo; Anding, Peter; Porcelli, Steven; Kaufmann, Stefan H. E.; Munk, Martin E.
CORPORATE SOURCE: Department of Immunology, Max Planck Institute for Infection Biology, Berlin, 10117, Germany
SOURCE: Infection and Immunity (2000), 68(10), 6073-6076
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nos. of gamma interferon (IFN-.gamma.)-producing cells reactive to ESAT-6 antigen were increased in recent converters to purified protein deriv. positivity and in tuberculosis patients but not in unvaccinated or Mycobacterium bovis BCG-vaccinated healthy donors. ESAT-6-reactive IFN-.gamma.-producing cells in recent converters and tuberculosis patients recognized similar synthetic peptides. Thus, ESAT-6 is a potential candidate for use in detection of early, as well as active, tuberculosis and for control of the disease.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 28 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:127366 CAPLUS
DOCUMENT NUMBER: 130:324082
TITLE: Immunological evaluation of novel Mycobacterium tuberculosis culture filtrate proteins
AUTHOR(S): Weldingh, Karin; Andersen, Peter
CORPORATE SOURCE: Department of TB Immunology, Statens Serum Institut,

Copenhagen, DK-2300, Den.
SOURCE: FEMS Immunology and Medical Microbiology (1999), 23(2), 159-164
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Culture filtrate from Mycobacterium tuberculosis contains mols. which can promote protective immunity to tuberculosis in animal models. Six novel proteins in the region of 17-29 kDa were purified and investigated for their immunol. relevance in M. tuberculosis-infected mice, guinea pigs and tuberculosis patients. The proteins CFP17, CFP21, CFP25 and CFP29 were all identified as strong interferon-.gamma. inducers in M. tuberculosis-infected mice and in tuberculosis patients. The CFP21 protein is encoded in the genomic region RD-2 which is deleted from a no. of BCG strains and the diagnostic potential of this antigen was evaluated.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 29 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:168551 CAPLUS
DOCUMENT NUMBER: 126:156423
TITLE: Mycobacterium tuberculosis DNA sequences encoding immunostimulatory peptides for tuberculosis vaccines
INVENTOR(S): Nano, Francis E.
PATENT ASSIGNEE(S): University of Victoria, Can.; Nano, Francis E.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700067	A1	19970103	WO 1996-US10375	19960614
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9662805	A1	19970115	AU 1996-62805	19960614
US 6228371	B1	20010508	US 1997-990823	19971215
US 6572865	B1	20030603	US 2000-477135	20000103
US 2002172684	A1	20021121	US 2001-996634	20011128
US 2003049269	A1	20030313	US 2001-997181	20011128
US 2003049263	A1	20030313	US 2001-997182	20011128

PRIORITY APPLN. INFO.:
US 1995-254P P 19950615
WO 1996-US10375 W 19960614
US 1997-990823 A2 19971215
US 2000-477135 A3 20000103

AB Nucleotide sequences isolated from Mycobacterium tuberculosis which encode immunostimulatory peptides are disclosed. DNA contg. the nucleotide sequences can be incorporated into vectors for prodn. of the peptides by transformed cells; it can also be used as a source of primers for isolation and amplification of M. tuberculosis genes, or of probes for detection of M. tuberculosis by hybridization assays. The peptides can be used in vaccines against tuberculosis, in immunoassays, and in tuberculin skin tests.

L80 ANSWER 30 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:364667 CAPLUS
DOCUMENT NUMBER: 127:32565
TITLE: Characterization of the delayed type hypersensitivity-inducing epitope of MPT64 from Mycobacterium tuberculosis
AUTHOR(S): Oettinger, T.; Holm, A.; Hasloev, K.
CORPORATE SOURCE: TB Research Unit, Department of Mycobacteriology, Statens Serum Institut, Copenhagen, DK-2300, Den.
SOURCE: Scandinavian Journal of Immunology (1997), 45(5), 499-503
CODEN: SJIMAX; ISSN: 0300-9475
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mycobacterium tuberculosis secretes several proteins into the extracellular environment, some of which are restricted to the M. tuberculosis complex. One of these antigens is MPT64. Recently, the authors showed that native as well as recombinant MPT64 is able to distinguish between an M. tuberculosis infection and a BCG Danish 1331 vaccination. Improved distinction between tuberculin purified protein deriv. (PPD) sensitivity conferred by an M. tuberculosis infection and that induced by a BCG vaccination or infection with environmental mycobacteria would be useful in the control of tuberculosis. In this study, the authors report the mapping and characterization of a Dth-inducing epitope by the use of synthetic peptides in guinea-pigs vaccinated with BCG Danish 1331 or Tokyo. Studies with overlapping synthetic peptides have pinpointed the biol. activity to a single Dth-inducing epitope at the C-terminal region of MPT64 consisting of 15 residues between amino acids Gly-173 and Ala-187, the core epitope (CE15). A fine mapping using truncated versions of CE15 indicates the epitope is restricted to 13 residues between amino acids Val-174 to Glu-186. However, the optimal Dth reactivity is obtained by CE15. Different modifications of CE15 revealed that a lysine tree construction improves the skin reactivity to a max. level approaching that of the reactivity to tuberculin PPD.

L80 ANSWER 31 OF 62 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:290377 CAPLUS
DOCUMENT NUMBER: 138:286120
TITLE: Vaccine preparation from a protein antigen from Mycobacterium tuberculosis
INVENTOR(S): Jagannath, Chinnaswamy; Balganesh, Meenakshi; Srinivasa, Bachally Ramasastry
PATENT ASSIGNEE(S): Astra Research Centre India, India
SOURCE: Indian, 28 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 175900	A	19951021	IN 1993-MA258	19930412

PRIORITY APPLN. INFO.: IN 1993-MA258 19930412
AB A 17-kiloDalton protein has been isolated from M. tuberculosis (South Indian Isolate-1) and sequenced. This 131-amino acid protein and fragments thereof including amino acids 68-77, 91-101 and/or 107-122; antibodies to the protein and the fragments; and DNA encoding the protein or fragments, or DNA hybridizable to such DNA are of interest in

immunodiagnosis, therapy, and vaccination in relation to human tuberculosis. The antigen had a sensitivity of 70% and a specificity of 85% in a micro ELISA for antibodies in human serum.

L80 ANSWER 32 OF 62 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2001188270 EMBASE
TITLE: Biotechnology in the development of new vaccines and diagnostic reagents against tuberculosis.
AUTHOR: Mustafa A.S.
CORPORATE SOURCE: A.S. Mustafa, Department of Microbiology, Faculty of Medicine, Kuwait University, P.O. Box 24923, Safat 13110, Kuwait. abusalim@hsc.kuniv.edu.kw
SOURCE: Current Pharmaceutical Biotechnology, (2001) 2/2 (157-173). Refs: 120
ISSN: 1389-2010 CODEN: CPBUBP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tuberculosis (TB) is a disease of global concern. About one third of the world populations is infected with Mycobacterium tuberculosis. Every year, approximately 8 million people get the disease and 2 million die of TB. The currently available vaccine against TB is the attenuated strain of Mycobacterium bovis, Bacillus Calmette Guerin (BCG), which has failed to provide consistent protection in different parts of the world. The commonly used diagnostic reagent for TB is the purified protein derivative (PPD) of M. tuberculosis, which is nonspecific because of the presence of antigens crossreactive with BCG and environmental mycobacteria. Thus there is a need to identify M. tuberculosis antigens as candidates for new protective vaccines and specific diagnostic reagents against TB. By using the techniques of recombinant DNA, synthetic peptides, antigen-specific antibodies and T cells etc., several major antigens of M. tuberculosis have been identified, e.g. heat shock protein (hsp)60, hsp70, Ag85, ESAT-6 and CFP10 etc. These antigens have shown promise as new candidate vaccines and/or diagnostic reagents against TB. In addition, recent comparisons of the genome sequence of M. tuberculosis with BCG and other mycobacteria have unraveled M. tuberculosis specific regions and genes. Expression and immunological evaluation of these regions and genes can potentially identify most of the antigens of M. tuberculosis important for developing new vaccines and specific diagnostic reagents against TB. Moreover, advances in identification of proper adjuvant and delivery systems can potentially overcome the problem of poor immunogenicity/short-lived immunity associated with protein and peptide based vaccines. In conclusion, the advances in biotechnology are contributing significantly in the process of developing new protective vaccines and diagnostic reagents against TB.

L80 ANSWER 33 OF 62 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 1998239322 EMBASE
TITLE: T-cell recognition of mycobacterial proteins MPB70 and MPB64 in cattle immunized with antigen and infected with Mycobacterium bovis.
AUTHOR: Lightbody K.A.; Girvin R.M.; Mackie D.P.; Neill S.D.; Pollock J.M.
CORPORATE SOURCE: K.A. Lightbody, Veterinary Sciences Division, Dept. of

Agric., Northern Ireland, Stoney Road, Stormont, Belfast BT4 3SD, United Kingdom
SOURCE: Scandinavian Journal of Immunology, (1998) 48/1 (44-51).
Refs: 34
ISSN: 0300-9475 CODEN: SJIMAX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Defined antigenic reagents and knowledge of T-cell responses are required for the design of improved diagnostic tests for bovine tuberculosis. The limited species distribution of Mycobacterium bovis antigens MPB70 and MPB64 has indicated their potential for inclusion in future tests. The strategy adopted in this study was to define bovine T-cell responses to these antigens at the epitope level, using cattle immunized with recombinant forms of the antigens, and to compare these responses with cattle which had been experimentally infected with M. bovis. Panels of synthetic peptides (20-mers with 10-residue overlaps) were used and five epitopes were identified and found to be powerful stimulators of T-cell responses in both types of animal (residues 81-100 and 174-190 for MPB70; and residues 1-20, 41-60 and 181-200 for MPB64). Further investigation in larger numbers of cattle (n = 14) of mixed breeds from tuberculosis-infected herds confirmed that each peptide produced response in several of the cattle, but no single peptide was recognized by all animals. However, the limited numbers of animals in this study suggest that peptide reagents may identify as many positive animals as the intact antigenic protein and could form components of a future diagnostic test. The use of cattle immunized with the proteins of interest has proved to be an interesting model for studying the nature of bovine T-cell responses to defined mycobacterial proteins.

L80 ANSWER 34 OF 62 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 96146206 EMBASE
DOCUMENT NUMBER: 1996146206
TITLE: T-cell response to mycobacterial proteins: A comparative study of tuberculous and control immunoblots of Mycobacterium tuberculosis and M. Bovis BCG.
AUTHOR: Bassey E.O.E.; Life P.F.; Catty D.; Gaston J.S.H.; Kumararatne D.S.
CORPORATE SOURCE: Pathobiological Sciences, Veterinary School, University of Wisconsin,Madison, WI 53706, United States
SOURCE: Tubercle and Lung Disease, (1996) 77/2 (146-153).
ISSN: 0962-8479 CODEN: TLDIEP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: English
SUMMARY LANGUAGE: English; French; Spanish
AB Objective: To evaluate and compare the lymphoproliferative response of human peripheral blood mononuclear cells (PBMC) to fractionated soluble extracts of Mycobacterium tuberculosis H37Rv (MTSE) and M. bovis bacille Calmette-Guerin (BCG) (MBSE), and thereby determine responses that correlate to infection, and to contrast antibody and T-cell responses. Design: Membrane blots of SDS-PAGE fractionated M. tuberculosis H37Rv and M. bovis BCG were employed for antibody immunoblotting and T-cell proliferative responses using sera and PBMC from seven tuberculous and seven BCG vaccinated control subjects. Results: The profiles of responses contrasted rather interestingly, with antibody and T-cells responding more to higher and lower molecular weight fractions respectively. T-cells

responding to antigens in the 59-88 kDa region discriminated between tuberculous and BCG vaccinated controls ($P < 0.05$) even though the differences were more toward the 70-75 kDa fractions within the region in question. Responses to smaller molecular weight fractions of both MTSE and MBSE were high in direct contrast to antibody responses. Additionally, responses to MBSE in these regions were generally higher than for MTSE in vaccinated controls. The reverse was the case with tuberculous subjects where responses to MTSE were generally higher, though not sufficiently significant in enough of the tuberculous subjects to be considered discriminatory. Conclusion: T-cell proliferative responses to mycobacterial antigens in the 59-88 kDa region, and particularly antigens in the 70-75 kDa region, can be an indication of infection with M. tuberculosis, as well as the basis for discriminating between active disease and vaccination with BCG.

L80 ANSWER 35 OF 62 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 95177668 EMBASE
DOCUMENT NUMBER: 1995177668
TITLE: Mapping of T cell epitopes of the 30-kDa .alpha. antigen of Mycobacterium bovis strain bacillus Calmette-Guerin in purified protein derivative (PPD)-positive individuals.
AUTHOR: Silver R.F.; Wallis R.S.; Ellner J.J.
CORPORATE SOURCE: Biomedical Research Building, 10W 10900 Euclid Avenue,Cleveland, OH 44106-4984, United States
SOURCE: Journal of Immunology, (1995) 154/9 (4665-4674). ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The fibronectin-binding 30-kDa .alpha. Ag is a major secretory protein of growing mycobacteria that stimulates in vitro lymphocyte blastogenesis in most healthy purified protein derivative-positive individuals, but only a minority of patients with active tuberculosis. T cell epitopes of the .alpha. Ag were assessed using blastogenic responses of PBMC from 12 healthy purified protein derivative-positive subjects to a set of synthetic peptides based on the 325-amino acid sequence of the .alpha. Ag of Mycobacterium bovis BCG. Because epitope-specific precursor cells are infrequent and randomly distributed, we used Poisson analysis to determine positive responses to 10 .mu.g/ml of each peptide in 12 replicate culture wells. Seven immunodominant regions of the .alpha. Ag were identified. Each subject responded to at least one of the two most dominant epitopes, which correspond to amino acids 131-155 and 233-257 (from N terminus). Peptides of these two epitopes induced production of IFN-.alpha. by sorted CD4+ T cells. The immunodominant peptides may have use as components of a vaccine and as tools to study the evolution of the immune response to M. tuberculosis. The two most dominant epitopes both occur in regions of the .alpha. Ag that differ from those of the atypical pathogens M. avium and M. kansasii. In addition, the M. bovis epitope of amino acids 133-155 differs from that of M. tuberculosis by a single amino acid. It may be possible to exploit the sequence differences for development of diagnostic tests with increased specificity.

L80 ANSWER 36 OF 62 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:69644 BIOSIS
DOCUMENT NUMBER: PREV200300069644
TITLE: Tuberculin skin testing and in vitro **T cell** responses to ESAT-6 and culture filtrate protein 10 after infection with Mycobacterium marinum or M. kansasii.

AUTHOR(S): Arend, Sandra M. (1); van Meijgaarden, Krista E.; de Boer, Kirsten; de Palou, Elisabeth Cerda; Van Soolingen, Dick; Ottenhoff, Tom H. M.; van Dissel, Jaap T.
CORPORATE SOURCE: (1) Dept. of Infectious Diseases, Leiden University Medical Center, C5P, 2300 RC, PO Box 9600, Leiden, Netherlands: s.m.arend@lumc.nl Netherlands
SOURCE: Journal of Infectious Diseases, (15 December 2002) Vol. 186, No. 12, pp. 1797-1807. print.
ISSN: 0022-1899.
DOCUMENT TYPE: Article
LANGUAGE: English
AB **T cell** responses to ESAT-6 and culture filtrate protein 10 (CFP-10), antigens expressed by Mycobacterium tuberculosis but not by M. bovis bacille Calmette-Guerin (BCG), were found to discriminate reliably between infection with M. tuberculosis and BCG vaccination. Because the esat-6 and cfp-10 genes occur in M. kansasii and M. marinum, **T cell** responses to ESAT-6 and CFP-10 were investigated in patients infected with M. kansasii or M. marinum, persons intensively exposed to environmental mycobacteria, and unexposed control subjects. Tuberculin skin tests were performed, and peripheral blood mononuclear cells were cocultured with ESAT-6, CFP-10, **peptide** mixtures of ESAT-6 and CFP-10, and control antigens. When enzyme-linked immunosorbent assay (ELISA) and enzyme-linked immunospot assay (ELISPOT) were used to measure interferon-gamma production, most M. kansasii- or M. marinum-infected patients and several persons exposed to environmental mycobacteria were found to respond to ESAT-6 and/or CFP-10. ELISA and ELISPOT yielded comparable results, as did whole antigen and **peptides** (P<.0001). These results may be relevant for the development of novel assays for **diagnosis** of **tuberculosis**.

L80 ANSWER 37 OF 62 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:599122 BIOSIS
DOCUMENT NUMBER: PREV200200599122
TITLE: Development of new vaccines and diagnostic reagents against tuberculosis.
AUTHOR(S): Mustafa, Abu Salim (1)
CORPORATE SOURCE: (1) Department of Microbiology, Faculty of Medicine, Kuwait University, P.O. Box 24923, Safat, 13110: abusalim@hsc.kuniv.edu.kw Kuwait
SOURCE: Molecular Immunology, (September, 2002) Vol. 39, No. 1-2, pp. 113-119. http://www.elsevier.com/locate/molimm. print.
ISSN: 0161-5890.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Tuberculosis (TB) is a major infectious disease problem with one-third of the world population infected, 8 million people developing the active disease and 2 million dying of TB each year. The attenuated Mycobacterium bovis Bacillus Calmette Guerin (BCG) is the only available vaccine against TB. However, the trials conducted in different parts of the world have shown that this vaccine doe not provide consistent protection against TB. The purified protein derivative (PPD) of Mycobacterium **tuberculosis** is the commonly used reagent for the **diagnosis** of TB. However, PPD lacks specificity because of the presence of antigens crossreactive with M. bovis BCG and other mycobacteria. The studies to identify M. tuberculosis antigens and epitopes as candidates for new protective vaccines and specific diagnostic reagents against TB have led to the identification and characterization of several major antigens of M. tuberculosis including heat shock proteins (hsp) and secreted antigens present in the culture filtrate (CF) of M. tuberculosis. Some of these antigens have shown promise as new candidate

vaccines (hsp60, Ag85 and ESAT-6, etc.) and specific diagnostic reagents (ESAT-6 and CFP10, etc.) for TB. Moreover, in the mouse model of TB, vaccination with DNA-hsp60 has immunotheraputic effects and helps in eradication of persisters. In addition, identification of proper adjuvant and delivery systems has shown the promise to overcome the problem of poor immunogenicity associated with subunit and **peptide** based vaccines. More recently, the comparison of the genome sequence of M. tuberculosis with M. bovis BCG and other mycobacteria has led to the identification of M. tuberculosis-specific genomic regions. Evaluation of these regions for encoding proteins with immunological reactivity can lead to the identification of additional antigens of M. **tuberculosis** useful as new vaccines and reagents for specific **diagnosis** of TB.

L80 ANSWER 38 OF 62 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:60354 BIOSIS
DOCUMENT NUMBER: PREV199900060354
TITLE: Differential **T cell** responses to Mycobacterium tuberculosis ESAT6 in tuberculosis patients and healthy donors.
AUTHOR(S): Ulrichs, Timo; Munk, Martin E. (1); Mollenkopf, Hans; Behr-Perst, Susanne; Colangeli, Roberto; Gennaro, Maria Laura; Kaufmann, Stefan H. E.
CORPORATE SOURCE: (1) Max-Planck-Inst. Infection Biol., Monbijoustr. 2, D-10117 Berlin Germany
SOURCE: European Journal of Immunology, (Dec., 1998) Vol. 28, No. 12, pp. 3949-3958.
ISSN: 0014-2980.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Vaccination against and **diagnosis** of **tuberculosis** are still insufficient. Proteins secreted by Mycobacterium **tuberculosis** induce strong immune responses in tuberculosis and constitute prime candidates for development of novel vaccines against tuberculosis as well as for immunodiagnostic assays. We investigated the role of the secreted proteins MPT63, MPT64 and ESAT6 from M. tuberculosis in healthy individuals and tuberculosis patients. None of the secreted proteins stimulated peripheral blood mononuclear cells from healthy donors. In contrast, CD4+ **T cells** from many tuberculosis patients were stimulated in an MHC class II-restricted fashion by ESAT6, but not by MPT63 or MPT64. **T cell** reactivities of tuberculosis patients were focused on the N-terminal region of ESAT6. The ESAT6 **T cell** epitopes were presented by different HLA-DR phenotypes. Cell cultures responding to either ESAT6 or synthetic **peptides** thereof showed mRNA transcripts for macrophage inflammatory protein (MIP)-1 alpha, monocyte chemotactic protein (MCP)-1 or IL-8 and production of IFN-gamma and MIP1alpha. Our results suggest that the secreted M. tuberculosis proteins MPT63, MPT64 or ESAT6 do not stimulate unprimed **T cells** , and that ESAT6 may be a potential candidate antigen for detection of clinical disease.

L80 ANSWER 39 OF 62 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:500168 BIOSIS
DOCUMENT NUMBER: PREV199396124175
TITLE: Recognition of **peptide** epitopes of the 16000 MW antigen of Mycobacterium tuberculosis by murine **T cells**.
AUTHOR(S): Vordermeier, H.-M.; Harris, D. P.; Lathigra, R.; Roman, E.; Moreno, C.; Ivanyi, J. (1)
CORPORATE SOURCE: (1) MRC Tuberculosis, Related Infections Unit, Hammersmith

Hosp., DuCane Road, London W12 0HS UK
SOURCE: Immunology, (1993) Vol. 80, No. 1, pp. 6-12.
ISSN: 0019-2805.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The **T-cell** repertoire to a prominent immunogen of Mycobacterium tuberculosis has been investigated on the assumption that differences in epitope specificity could influence the protective and pathogenic host reactions. Proliferative responses of lymph node and spleen cells to overlapping **peptides**, spanning the entire sequence of the 16,000 MW protein antigen were analysed in C57BL/10 and B10.BR mice. Following footpad priming and in vitro challenge with homologous **peptide**, 12 out of the 14 **peptides** tested were found to be immunogenic. However, only two **peptides** of residues 31-40 and 71-91 stimulated strong proliferative responses of **T cells** from mice which had been presensitized with either killed or live M. tuberculosis organisms: another three **peptides** were only weakly stimulatory. These epitopes have been immunodominant in both H-2-b and H-2-k mouse strains, indicating the genetically permissive nature of their recognition: Furthermore, both major immunodominant epitopes were found to be species specific for the M. **tuberculosis** complex and therefore potentially suitable for the early **diagnosis** of tuberculous infection.

L80 ANSWER 40 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-278351 [27] WPIDS
DOC. NO. NON-CPI: N2003-221111
DOC. NO. CPI: C2003-072684
TITLE: Oligonucleotides for detecting tubercle bacillus via its pab genes after cleavage, amplification and identification, applicable particularly in combination for quantitation of **Mycobacterium tuberculosis** and in **diagnosis**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): ISHIGURO, T; MARUYAMA, T; MASUDA, N; MATSUBA, T; TSUCHIYA, S
PATENT ASSIGNEE(S): (TOYJ) TOSOH CORP
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003010309	A1	20030206	(200327)*	JA	52
RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR					
W: CN KR SG US					
JP 2003033182	A	20030204	(200327)		11
JP 2003047478	A	20030218	(200327)		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003010309	A1	WO 2002-JP7508	20020724
JP 2003033182	A	JP 2001-224436	20010725
JP 2003047478	A	JP 2001-240874	20010808

PRIORITY APPLN. INFO: JP 2001-240874 20010808; JP 2001-224436 20010725
AB WO2003010309 A UPAB: 20030429

NOVELTY - Oligonucleotides comprising not less than 10 consecutive bases in the sequences of (I)-(XX) with 20-23 base pairs for use in cleaving, detecting or amplifying essential pab genes of tubercle bacillus or RNA originated from them and capable of binding specifically with such genes or RNA, or their complementary oligonucleotides, are new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for the detection of tubercle bacillus-originated pab genes comprising:

(a) using specific sequences of the pab genes or their derived RNA in a sample as template, and a first primer containing sequences analogous to such specific sequences and a second primer containing sequences complementary to these specific sequences (provided that any of the first and second primers has a sequence attached with a promoter sequence of RNA polymerase at its 5'-side), with RNA-dependent DNA polymerase for cDNA synthesis, and producing single-stranded DNA by decomposition of the RNA of an RNA-DNA double strand by ribonuclease H;

(b) using the single-stranded DNA as template for DNA-dependent DNA polymerase to form a double-stranded DNA with a promoter sequence for transcription of an RNA from the specific sequences or their complementary sequences and subsequently producing an RNA product in the presence of an RNA polym erase with the double-stranded DNA;

(c) RNA amplification with such RNA transcription product as template for cDNA synthesis by the RNA-dependent DNA polymerase, wherein the first and second primers can also be those of not less than 10 bases long derived from sequences (XXVIII)-(XXXIII) all with 51 base pairs and from sequences (XXXIV)-(XLI) with 20-23 base pairs, identical to a part of the RNA sequence originating in the pab genes or their complementary sequences, for amplification.

USE - The oligonucleotides are useful for detecting tubercle bacillus, which is applicable particularly in combination for quantitation of **Mycobacterium tuberculosis** and in its **diagnosis.**

ADVANTAGE - The oligonucleotides can be used in the sensitive identification of tubercle bacillus-originated antigen **proteins** or RNA-originated from these genes.

Dwg.0/3

L80 ANSWER 41 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-583530 [62] WPIDS
DOC. NO. NON-CPI: N2002-462760
DOC. NO. CPI: C2002-164954
TITLE: Identifying an anti-**mycobacterial** agent that modulates activity/expression of a **protein** expressed by **Mycobacterium**, involves monitoring the effect of an agent on the activity/expression of the **protein** or polynucleotide/vector encoding it.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): CALVIN, B K K; DICK, T
PATENT ASSIGNEE(S): (MOLE-N) INST MOLECULAR & CELL BIOLOGY
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002048391	A2	20020620	(200262)*	EN	56

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

ZW
AU 2002016100 A 20020624 (200267)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002048391	A2	WO 2001-EP14551	20011211
AU 2002016100	A	AU 2002-16100	20011211

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002016100	A	Based on	WO 200248391

PRIORITY APPLN. INFO: GB 2000-30368 20001213

AB WO 200248391 A UPAB: 20020926
NOVELTY - Identifying (M1) anti-**mycobacterial** agent that modulates activity and/or expression of **protein** (I) expressed by **Mycobacterium** in non-oxygen limiting or hypoxic stationary, hypoxic growth phase, involves contacting a **test** agent and (I), its variant, their fragments or polynucleotide/vector encoding (I), and monitoring the effect of agent on activity/expression of (I).

DETAILED DESCRIPTION - Identifying (M1) anti-**mycobacterial** agent that modulates activity and/or expression of **protein** (I) expressed by **Mycobacterium** in non-oxygen limiting or hypoxic stationary, hypoxic growth phase, involves contacting a **test** agent and (I) (such as Rv3133c, Rv26233 or Rv2626c), its variant, their fragments or polynucleotide/vector encoding (I), and monitoring the effect of agent on activity/expression of (I).

INDEPENDENT CLAIMS are also included for the following:

(1) identifying (M2) diagnostic agent that binds to (I), or a polynucleotide encoding (I), involves contacting **test** agent and (I), its variant, their fragments, or polynucleotide/vector encoding (I), and monitoring any interaction between the **test** agent and (I) or the polynucleotide;

(2) an agent (II) which is identifiable by (M1) or (M2);

(3) an antibody (III) specific for (I);

(4) a pharmaceutical composition (IV) comprising (II) or (III), as an active ingredient;

(5) a vaccine composition (V) comprising (I), and its variant or immunogenic fragment, as an active ingredient;

(6) preventing (M3) a **mycobacterial** infection in a subject, involves administering (I), its variant or fragment, (II), (III) or (V), to the subject; and

(7) obtaining (M4) (I) or its variant, involves maintaining **Mycobacterium** under aerobic or anaerobic conditions suitable for inducing non-oxygen limiting stationary phase, hypoxic stationary or growth phase expressed **proteins**, and isolating the **proteins**.

ACTIVITY - Tuberculostatic.
No suitable data given.

MECHANISM OF ACTION - Vaccine; Modulator of activity and/or expression of (I) (claimed).

USE - (II)-(V) are useful for treating a human or animal body by therapy, in a diagnostic method practiced on the human or animal body, and for manufacturing medicament for **diagnosis**, prophylaxis or treatment of **mycobacterial** infection, especially **tuberculosis**. (II) or (III) is useful for in vitro or in vivo diagnosing of **mycobacterial** infection in a sample. The method

involves detecting the presence of (I) or its variant, or a nucleic acid (DNA) encoding (I), by determining the binding of (II) or (III) to the sample, or detecting the response to (II) or (III), by monitoring expression of (I) or its variant. (I), its fragment, variant or fragment of the variant, is useful for identifying anti-**mycobacterial** agents, and as an agent for diagnosing a dormant **mycobacterial** infection. (claimed). (III) is useful for detecting, purifying and isolating (I).
Dwg.0/7

L80 ANSWER 42 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-147798 [19] WPIDS
DOC. NO. CPI: C2002-045868
TITLE: Composition comprising MTB39 antigen and MTB32A antigen from **Mycobacterium** species, useful for eliciting immune response in a subject.
DERWENT CLASS: B04 D16
INVENTOR(S): ALDERSON, M; REED, S; SKEIKY, Y
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001098460	A2	20011227	(200219)*	EN	136
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001068678	A	20020102	(200230)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001098460	A2	WO 2001-US19959	20010620
AU 2001068678	A	AU 2001-68678	20010620

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001068678	A Based on	WO 200198460

PRIORITY APPLN. INFO: US 2001-265737P 20010201; US 2000-597796 20000620

AB WO 200198460 A UPAB: 20020321
NOVELTY - A composition (I) comprising a MTB39 antigen (A1) (comprising a sequence of 263 or 391 amino acids fully defined in the specification) and a MTB32A antigen (A2) (comprising a sequence of 355 or 330 amino acids fully defined in the specification), or their immunogenic fragments, from a **Mycobacterium** sp. of the tuberculosis complex, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an expression cassette (II) comprising a nucleic acid encoding A1 and a nucleic acid encoding A2;
(2) an isolated nucleic acid (III) encoding (II), where at least one amino acid in the active site triad of the MTB32A antigen has been substituted by a different amino acid;

(3) an isolated nucleic acid (IIIa) encoding a fusion polypeptide comprising (III);

(4) an isolated MTB32A polypeptide (IV) from a **Mycobacterium** sp. of the tuberculosis complex, has at least one amino acid in the active site triad of the MTB32A antigen substituted by a different amino acid;

(5) a fusion polypeptide (FP1) comprising (IV);

(6) an isolated nucleic acid (V) encoding a fusion polypeptide comprising A1 and an antigen comprising at least 195 amino acids from the N-terminus of (IV);

(7) a nucleic acid encoding a fusion polypeptide comprising (V);

(8) an isolated polypeptide (VI) encoding a fusion polypeptide comprising A1 and an antigen comprising at least 195 amino acids from (IV);

(9) a fusion polypeptide (FP2) comprising (Va); and

(10) a composition (C) comprising (III), (IV), (V) or (VI).

ACTIVITY - Tuberculostatic; immunostimulant.

MECHANISM OF ACTION - Vaccine.

Guinea pigs were immunized with adjuvants (SBAS1, SBAS2 or ASAS7 plus Al(OH)3), MTB72F fusion **protein** in adjuvant, or TbH9 plus Ra35 antigen composition at a dosage of 4 micro g each of TbH9 and Ra35, and 8 micro g of MTB72F. Second immunization was carried out after 3 weeks and third immunization approximately after two and a half weeks. 10 micro g of antigen was used as a prechallenge to determine antigenicity and delayed type hypersensitivity (DTH). Weight loss and death of the animals were monitored. The results for DTH were positive to the immunizing antigens. Reactions to individual antigens or the fusion **protein** were comparable. Guinea pigs vaccinated with MTB72F fusion **protein** afforded protection compared to those immunized with a mixture of antigens.

USE - (I) and (II) are useful for eliciting an immune response in a mammal, e.g., human, immunized with BCG (claimed). (I) and (II) are useful in diagnosis, treatment and prevention of **Mycobacterium** infection. (I), the fusion **proteins** and the polynucleotides are useful as diagnostic tools in patients infected with **Mycobacterium** , in vitro and in vivo **assays** for detecting humoral antibodies or cell-mediated immunity against M. **tuberculosis** for **diagnosis** of an infection or monitoring of disease progression, as immunogens to generate or elicit a protective immune response in a patient and for raising anti-M. tuberculosis antibodies in a non-human animal. (IV) is useful as in vivo diagnostic agent for intradermal skin **test**.

ADVANTAGE - Compositions and fusion **proteins** /polynucleotides that contain at least two heterologous M. tuberculosis coding sequences or antigens are highly antigenic and upon administration to a patient increase the sensitivity of tuberculosis sera.

Monkeys immunized with a composition comprising a mixture of two antigens (MTB72F and MTB8.4) showed weight stabilization and low erythrocyte sedimentation rate (ESR) (max 10) compared to those immunized with single antigen (MTB8.4) which showed weight loss and high ESR (max 30).

Dwg.0/7

L80 ANSWER 43 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-091923 [10] WPIDS
DOC. NO. CPI: C2001-027205
TITLE: New polypeptide encoded by a member of the esat-6-gene family for immunizing against and **diagnosis** of **tuberculosis**.
DERWENT CLASS: B04 D16
INVENTOR(S): ANDERSEN, P; SKJOT, R
PATENT ASSIGNEE(S): (STAT-N) STATENS SERUM INST

COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004151	A2	20010118	(200110)*	EN	57
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000059664	A	20010130	(200127)		
EP 1200466	A2	20020502	(200236)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003510018	W	20030318	(200321)		96

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004151	A2	WO 2000-DK398	20000713
AU 2000059664	A	AU 2000-59664	20000713
EP 1200466	A2	EP 2000-945660	20000713
		WO 2000-DK398	20000713
JP 2003510018	W	WO 2000-DK398	20000713
		JP 2001-509760	20000713

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000059664	A	Based on	WO 200104151
EP 1200466	A2	Based on	WO 200104151
JP 2003510018	W	Based on	WO 200104151

PRIORITY APPLN. INFO: US 1999-144011P 19990715; DK 1999-1020 19990713

AB WO 200104151 A UPAB: 20010220
NOVELTY - A polypeptide fragment (I) which comprises an amino acid sequence encoded by a member of the esat-6-gene family or comprises an amino acid analogue having a sequence identity of 70% and immunological equivalence to the polypeptide encoded by a member of the esat-6-gene family, is new.

DETAILED DESCRIPTION - A polypeptide fragment (I) which comprises an amino acid sequence encoded by a member of the esat-6-gene family or comprises an amino acid analogue having a sequence identity of 70% and immunological equivalence to the polypeptide encoded by a member of the esat-6-gene family, is not selected from Rv0287, Rv0288, Rv1037c, Rv1038c, Rv1197, Rv1198, Rv1792, Rv1793, Rv2346c, Rv2347c, Rv3019c, Rv3619c, Rv3620c, Rv3874 and Rv3875.

INDEPENDENT CLAIMS are also included for the following:

(1) a fusion polypeptide comprising (I) and at least one fusion partner;

(2) a vaccine for immunizing an animal, including a human, against tuberculosis (TB) caused by **mycobacteria** belonging to the TB complex, comprises a non-pathogenic microorganism, where at least one copy of a DNA fragment comprising the sequence encoding (I) has been incorporated into the genome of the microorganism, for expression and secretion of the polypeptide;

(3) an immunologic composition comprising (I);

(4) an isolated nucleic acid fragment (II) which comprises a member of the esat-6-gene family, and has a length of at least 10 nucleotides and hybridizes with a nucleic acid fragment comprising a sequence selected from 339, 327, 324, 246, 294, 303, 378, 288, 324, 273, 312 base pairs (bp) given in the specification;

(5) a vaccine comprising (II) which effects in vivo expression of antigen by an animal, which confers resistance to infections with **mycobacteria** of the TB complex;

(6) a replicable expression vector (III) which comprises (II);

(7) a transformed cell harboring at least one (III);

(8) a method for producing an immunologic composition (X) comprising solubilizing or dispersing (I) in a vaccine medium and optionally adding other M. tuberculosis antigens and/or a carrier, vehicle and/or adjuvant substance, or cultivating a cell and transferring the cell to a vaccine medium and optionally adding a carrier, vehicle and/or adjuvant substance; and

(9) a monoclonal or polyclonal antibody, which specifically reacts with (I) in an immunoassay, or a specific binding fragment of the antibody.

ACTIVITY - Tuberculostatic.

MECHANISM OF ACTION - Vaccine.

The antigens (TB7.3, TB10.4 and CFP10, which are members of the ESAT-6 family) were investigated in 13-17 tuberculosis (TB) patients, 4-7 Bacille Calmette Guerin (BCG) vaccinated and 7 non-vaccinated donors. TB7.3 was recognized at low levels in both the patients and BCG vaccinated donors. TB10.4 however, was recognized at a much higher level. In the TB patients, CFP10 induced a pronounced release of interferon- gamma (INF-gamma). Compared to ESAT6, TB100.4 induced significantly higher levels of INF- gamma in TB patients, whereas T cell responses to CFP10 and ESAT-6 were similar. Both CFP10 and TB10.4 were recognized by greater than 70% of the TB patients. The results demonstrate that the ESAT-6 family contain a number of molecules of potential relevance for TB vaccines and diagnostics.

USE - (I) and (II) can be used as pharmaceuticals or in the preparation of pharmaceutical compositions for the **diagnosis** of or vaccination against TB caused by M. **tuberculosis**, M. africanum or M. bovis. **Diagnosis** of TB comprises intradermally injecting (I) alone or in a composition, a positive skin response at the location is an indication of the animal having TB. Diagnosing ongoing or previous sensitization in an animal with bacteria belonging to the TB complex, involves contacting a blood sample with (I), a significant release into the extracellular phase of a cytokine by mononuclear cells is an indication of sensitization. Immunizing an animal against TB comprises administering (I) alone, or in a composition or vaccine (claimed).

Dwg.0/6

L80 ANSWER 44 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-579445 [54] WPIDS
DOC. NO. NON-CPI: N2000-428766
DOC. NO. CPI: C2000-172545
TITLE: New nucleic acid sequences that are deleted from the genome of **Mycobacterium** bovis BCG but present in the genome of M. tuberculosis, useful as a vaccine against **mycobacteria**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BILLAULT, P; BUCHRIESER, B R; COLE, S; GARNIER, T; GOURDON, S; BILLAULT, A; BUCHRIESER-BROSCH, R; GORDON, S
PATENT ASSIGNEE(S): (INSP) INST PASTEUR
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000055362	A1	20000921	(200054)*	FR	95
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
FR 2791067	A1	20000922	(200054)		
AU 2000032989	A	20001004	(200101)		
EP 1161562	A1	20011212	(200204)	FR	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000055362	A1	WO 2000-FR637	20000316
FR 2791067	A1	FR 1999-3250	19990316
AU 2000032989	A	AU 2000-32989	20000316
EP 1161562	A1	EP 2000-910960	20000316
		WO 2000-FR637	20000316

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000032989	A	Based on	WO 200055362
EP 1161562	A1	Based on	WO 200055362

PRIORITY APPLN. INFO: FR 1999-3250 19990316

AB WO 200055362 A UPAB: 20001027

NOVELTY - Polynucleotide sequences (I) that are deleted from the genome of **Mycobacterium** bovis BCG (A) but present in the genome of M. tuberculosis, or vice versa, are new.

DETAILED DESCRIPTION - Polynucleotide sequences (I) that are deleted from the genome of **Mycobacterium** bovis BCG (A) but present in the genome of M. tuberculosis, or vice versa, are new.

(I) are the following genes or open reading frames (ORFs): Rv 2346c, 2347c, 2348c, 2352c, 2353c, 3425, 3426, 3427c, 3428c, 1964, 1965, 1967, 1968, 1969, 1971, 1972, 1973, 1974, 1975, 1976c, 1977, 3618, 3619c, 3620c, 3621c, 3622c, 2073c, 2074, 2075, 0223c, 2024c, or 1758; plcA, B, C or D; mce3; lprM; ephA; lpqG; cobL; echa1; RvD1-ORF1 or -ORF2; RvD2-ORF1, -ORF2 or -ORF3.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for detecting or discriminative identification of (A) and M. tuberculosis in a biological sample;

(2) kits for carrying out the method of (1);

(3) expression products (II) of all or part of (I);

(4) a process for discriminative identification in vitro of antibodies (Ab) directed against (A) or M. tuberculosis in a biological sample;

(5) process for discrimination between vaccination with M. bovis BCG and infection with M. tuberculosis;

(6) kit for in vitro **diagnosis** of M. **tuberculosis** infection in an animal optionally vaccinated with BCG;

(7) antibodies (Ab1), mono- or poly-clonal, that specifically recognize (II);

(8) a method for discriminating between presence of antibodies specific for (A) or M. tuberculosis in a biological sample;
(9) kit for carrying out the method of (8);
(10) immunogenic composition containing at least one (II);
(11) vaccine comprising the composition of (10); and
(12) a method for detecting and discriminative identification of BCG and M. tuberculosis in a biological sample.
ACTIVITY - Antibacterial.
MECHANISM OF ACTION - Induction of specific immune response; Vaccine.
No biological data given.
USE - Identification of (I) allows discrimination between M. tuberculosis and (A). The expression products (II) of (I) can be used similarly to differentiate between antibodies specific for (A) and M. tuberculosis, e.g. to distinguish between vaccination with BCG and tuberculosis, while antibodies (Ab1) raised against (II) can be used for differentiation between antigens of (A) and M. tuberculosis. (II) can also be used as immunogen, particularly in vaccines.
ADVANTAGE - (I) are specific for either (A) or M. tuberculosis.
Dwg.0/6

L80 ANSWER 45 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-638180 [61] WPIDS
DOC. NO. NON-CPI: N2000-473375
DOC. NO. CPI: C2000-191908
TITLE: Novel **Mycobacterium** tuberculosis polypeptide comprising an immunogenic portion of M. **tuberculosis** antigens Mtb-81 and Mtb-67.2, useful for **diagnosis**, treatment and monitoring therapy of **tuberculosis**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HENDRICKSON, R C; HOUGHTON, R L; LODES, M J
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP; (HEND-I) HENDRICKSON R C; (HOUG-I) HOUGHTON R L; (LODE-I) LODES M J
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000055194	A2	20000921	(200061)*	EN	91
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000040147	A	20001004	(200101)		
EP 1169342	A2	20020109	(200205)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
BR 2000009077	A	20020416	(200234)		
JP 2002543761	W	20021224	(200313)		116
US 2003027774	A1	20030206	(200313)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000055194	A2	WO 2000-US7196	20000317
AU 2000040147	A	AU 2000-40147	20000317
EP 1169342	A2	EP 2000-919461	20000317
		WO 2000-US7196	20000317
BR 2000009077	A	BR 2000-9077	20000317

	WO 2000-US7196	20000317
JP 2002543761 W	JP 2000-605620	20000317
	WO 2000-US7196	20000317
US 2003027774 A1	US 1999-272975	19990318

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000040147	A	Based on	WO 200055194
EP 1169342	A2	Based on	WO 200055194
BR 2000009077	A	Based on	WO 200055194
JP 2002543761	W	Based on	WO 200055194

PRIORITY APPLN. INFO: US 1999-272975 19990318

AB WO 200055194 A UPAB: 20001128

NOVELTY - A polypeptide (I) comprising an immunogenic portion of **Mycobacterium** tuberculosis antigens Mtb-81 or Mtb-67.2 which has a fully defined sequence (S1) of 606 amino acids, given in the specification, or a variant (VA) that differs in substitutions, additions, insertions and/or deletions such that ability of VA to react with antigen specific antisera or T-cells is not diminished, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) encoding (I);

(2) an antisense polynucleotide (III) comprising at least 15 consecutive nucleotides complementary to (S1);

(3) an expression vector (IV) comprising (II) or (III);

(4) a host cell (V) transformed or transected with (IV);

(5) an isolated antibody (VI) or antigen-binding fragment that specifically binds to Mtb-81 or Mtb-67.2;

(6) an antigen presenting cell (VII) that expresses (I);

(7) a diagnostic kit comprising (I), (II), or (VI) and a solid support;

(8) a fusion **protein** comprising (I) and a known M.tuberculosis antigen;

(9) a pharmaceutical composition comprising (I), (II), (VI) or (VII) and a carrier;

(10) a vaccine comprising (I), (II) or (VII) and a non-specific immune response enhancer;

(11) determining the presence or absence of M.tuberculosis in a biological sample comprising:

(i) contacting the sample with (I) or (VII);

(ii) detecting immunocomplexes formed between (I) and antibodies specific to (I); and

(iii) comparing the amount of immunocomplexes detected to a cut-off value;

(12) monitoring therapy in a patient infected by M. tuberculosis comprising:

(i) contacting a biological sample obtained from the patient at a first time point with (I) or (VII);

(ii) detecting immunocomplexes formed between (I) and antibodies specific to (I);

(iii) repeating (a) and (b) using a sample obtained at a second time point which follows a portion of therapy for M. tuberculosis infection; and

(iv) comparing the amount of immunocomplexes detected in (a) with those in (c);

(13) stimulating and/or expanding T cells specific for Mtb-81 comprising contacting T cells with (I), (II) or (IV);

(14) an isolated T cell population comprising T cells prepared by

(13);

(15) CD4+ and/or CD8+ T cells isolated from a patient and incubated with (I), (II), or (IV), such that the T cells proliferate and can be used in the manufacture of a medicament for inhibiting the development of tuberculosis in the patient;

ACTIVITY - Tuberculostatic. No suitable biological data is given.

MECHANISM OF ACTION - Mtb-81 or Mtb-67.2 T cell stimulator; vaccine. No suitable biological data is given.

USE - (I), expression vectors (VI) comprising (I) or an antisense polynucleotide, or an antigen presenting cell (VII) comprising (I) is useful for determining (D) the presence or absence of M.tuberculosis in whole blood, serum, sputum, plasma, saliva, cerebrospinal fluid or urine in a patient infected with human immunodeficiency virus (HIV). (I), (VI) or (VII) is also useful for monitoring therapy in a patient infected with M.tuberculosis. CD4+ and/or CD8+ T cells specific for Mtb-81 or Mtb-67.2 are stimulated and/or expanded by contacting with (I), a polynucleotide (II) encoding (I) and/or (VII). (I), (II) encoding (I), (VI), (VII) and the T cells are useful for the manufacture of a medicament for inhibiting the development of tuberculosis (claimed). (I), (VI) and (VII) are useful for detection, treatment, serodiagnosis and immunotherapy of tuberculosis.

ADVANTAGE - (I), a polynucleotide encoding (I) and expression vectors comprising (I) or an antisense polynucleotide may be used within a variety of serodiagnosis methods for tuberculosis detection and provides enhanced sensitivity in patients infected with human immunodeficiency virus.

Dwg.0/5

L80 ANSWER 46 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-533178 [48] WPIDS
DOC. NO. CPI: C2000-158913
TITLE: Nucleic acids encoding TANGO 228, 240 and 243 pp. which have homology to the rat mast cell Ag-32, the **Mycobacterium** tuberculosis hypothetical **protein** Rv0712 and human phospholipase A2-activating **protein**.
DERWENT CLASS: B04 D16
INVENTOR(S): FRASER, C C
PATENT ASSIGNEE(S): (MILL-N) MILLENNIUM PHARM INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000050443	A2	20000831	(200048)*	EN	188

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000033828 A 20000914 (200063)

EP 1179000 A2 20020213 (200219) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000050443	A2	WO 2000-US5035	20000225
AU 2000033828	A	AU 2000-33828	20000225
EP 1179000	A2	EP 2000-912028	20000225

WO 2000-US5035 20000225

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000033828	A	Based on	WO 200050443
EP 1179000	A2	Based on	WO 200050443

PRIORITY APPLN. INFO: US 1999-259387 19990226

AB WO 200050443 A UPAB: 20001001

NOVELTY - Nucleic acids (I) encoding secreted TANGO 228, 240 and 243 polypeptides (pp.) (II) which have homology to the rat mast cell Ag-32, the **Mycobacterium** tuberculosis hypothetical **protein** Rv0712 and human phospholipase A2-activating **protein** (respectively).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a nucleic acid molecule (NAM) (I) selected from:

(a) a NAM comprising (comp.) a nucleotide sequence (seq.) at least 55% identical to one of 6 defined seq. ((N1)-(N6)) given in the specification, the cDNA insert of plasmid ATCC 207116, or a complement (comp.) of them;

(b) a NAM comp. a 300 nucleotide fragment of (N1)-(N6), the cDNA insert of ATCC 207116, or a comp. of them;

(c) a NAM which encodes a pp. comp. one of 4 defined seq. ((A1)-(A4)) given in the specification, or the amino acid seq. encoded by the cDNA insert of ATCC 207116;

(d) a NAM which encodes a fragment of a pp. comp. 15 contiguous residues of (A1)-(A4) or the amino acid seq. encoded by the cDNA insert of ATCC 207116; and/or

(e) a NAM which encodes a naturally occurring allelic variant (NOAV) of a pp. comp. (A1)-(A4) or the seq. encoded by the cDNA insert of ATCC 207116 (the NAM hybridizes to a NAM comp. (N2), (N4) and/or (N6), or a comp., under stringent conditions);

(2) an isolated pp. (II) selected from:

(a) a fragment of a pp. comp. (A1)-(A4);

(b) a NOAV of a pp. comp. (A1)-(A4) or the amino acid seq. encoded by the cDNA insert of ATCC 207116 and which is encoded by a NAM which hybridizes to a nucleic acid molecule comp. (N2), (N4) and/or (N6) or a comp. under stringent conditions;

(c) a pp. which is encoded by a NAM comp. a seq. at least 55% identical to a NAM comp. the seq. (N2) and/or (N3) or at least 93% identical to a NAM comp. (N5) or a comp.;

(3) a host cell (III) comp. the NAM (I);

(4) an antibody (IV) that binds (II);

(5) a method (meth.) (V) for producing the pp. (II), comp. culturing the host cell (III) under conditions in which (I) is expressed;

(6) a meth. (VI) for detecting the presence of (II) in a sample, comp.:

(a) contacting (cont.) the sample with a compound (cmpd.) that selectively binds (II); and

(b) determining whether the cmpd. binds to pp. in the sample;

(7) a kit (VII) comp. a cmpd. that selectively binds to (II) and instructions for use;

(8) a meth. (VIII) for detecting the presence of (I) in a sample, comp.:

(a) cont. the sample with a nucleic acid probe or primer which selectively hybridizes to the NAM; and

(b) determining whether the nucleic acid probe or primer binds to a NAM in the sample;

(9) a kit (IX) comp. a cmpd. that selectively binds to (I) and instructions for use;

(10) a meth. (X) for identifying a cmpd. which binds to (II), comp.:

(a) cont. a pp. comp. (II) or cell expressing (II) with a **test** cmpd.; and

(b) determining whether the **test** cmpd. binds to (II);

(11) a meth. (XI) for modulating the activity of (II), comp. cont. (II) or a cell expressing (II) with a cmpd. that binds to (II) in a concentration that mod. the activity of (II); and

(12) a meth. (XII) for identifying a cmpd. which modulates (mod.) the activity of (II), comp.:

(a) cont. (II) with a **test** cmpd.; and

(b) determining the effect of the test cmpd. on the activity of (II) to identify a cmpd. which mod. the activity of (II).

ACTIVITY - None given.

MECHANISM OF ACTION - TANGO 228 has the ability to:

(1) modulate (mod.) protein-protein interactions and protein-ligand interactions;

(2) interact with antigens;

(3) initiate the immune response;

(4) mod. the activity of connective tissue cells;

(5) mod. intracellular signaling cascades by interacting with target peptides;

(6) mediate the allergic response;

(7) mod. lipid associated processes by interacting with a cell surface protein on a cell type involved in the immune response; and

(8) perform 1 or more of the functions of rat surface protein MCA-32.

TANGO 240 has the ability to:

(1) mod. the tuberculosis pathology pathway in the same fashion as Mycobacterium tuberculosis conserved hypothetical protein Rv0712; and

(2) mod. the function, migration, proliferation and/or differentiation of cells.

TANGO 243 has the ability to:

(1) mod. the activity of enzymes that hydrolyze lipids;

(2) mod. the activity of enzymes that release precursors of regulatory molecules associated with the arthropathy pathway; TAT mediate the arthropathy pathway;

(3) mod. the activity of cell types associated with the arthropathic pathway;

(4) mod. the synthesis of and/or release of, cell mediating molecules;

(5) mod. an immune and/or inflammatory response;

(6) mod. an immune and/or inflammatory response, in which TANGO 243 itself is stimulated by the cell mediating molecule that it mod.;

(7) mod. the activity of enzymes;

(8) mod. cell-cell interaction by modulating phospholipase A2 activation and/or signal transduction;

(9) mod. cell permeability;

(10) mod. cell-cell adhesion;

(11) mod. cellular functions;

(12) mod. signal transduction; and

(13) perform one or more of the functions of human PLAP.

No data given.

USE - (I) and (II) may be used in the prevention, treatment and diagnosis of diseases associated with inappropriate TANGO 228, 240 and 243 (collectively TANGO) expression and activity. For example, (I) (and vectors containing (I) (Iv)) and the TANGO pp. may be used to treat disorders associated with decreased TANGO expression. (I) or (Iv) may be administered to treat diseases by rectifying mutations or deletions in a patient's genome that affect the activity of TANGO by expressing inactive proteins or to supplement the patients own production of TANGO pp..

Additionally, (I) may be used to produce TANGO, according to standard recombinant DNA methodology, by inserting the nucleic acids into a host cell and culturing the cell to express the protein (meth. (V)). Conversely, antisense nucleic acid molecules (I') may be administered to down regulate TANGO expression by binding with the cells own TANGO genes and preventing their expression.

(I) and (I') may also be used as DNA probes in diagnostic assays (e.g. polymerase chain reactions) to detect and quantitate the presence of similar nucleic acid seq. in samples, and hence which patients may be in need of restorative therapy (i.e. meth. (VIII)).

They may also be used to study the expression and function of TANGO pp. and their role in metabolism through the production of transgenic animal models.

The TANGO pp. may be used as antigens in the production of antibodies (IV) against TANGO and in assays to identify modulators (agonists and antagonists) of TANGO expression and activity (meth. (X) and (XII)). The anti-TANGO antibodies and TANGO antagonists may also be used to down regulate TANGO expression and activity.

The anti-TANGO antibodies may also be used as diagnostic agents for detecting the presence of TANGO pp. in samples (e.g. by enzyme linked immunosorbant assay) (meth. (VI)).

Dwg.0/23

L80 ANSWER 47 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-601610 [51] WPIDS
CROSS REFERENCE: 1997-192903 [17]; 1998-251292 [22]; 1998-261042 [23]; 1999-527409 [44]; 2002-171134 [22]
DOC. NO. CPI: C1999-175166
TITLE: New fusion **proteins** useful for **diagnosis**, prevention and treatment of **tuberculosis**.
DERWENT CLASS: B04 D16
INVENTOR(S): ALDERSON, M; CAMPOS-NETO, A; SKEIKY, Y A W; SKEIKY, Y A; DILLON, D C; REED, S G; SKEIKY, Y.
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9951748	A2	19991014	(199951)*	EN	83
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9934817	A	19991025	(200011)		
EP 1068329	A2	20010117	(200105)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NO 2000005050	A	20001130	(200108)		
CZ 2000003652	A3	20010516	(200132)		
HU 2001001521	A2	20010828	(200157)		
BR 9909472	A	20010911	(200162)		
CN 1304451	A	20010718	(200163)		
KR 2001071138	A	20010728	(200208)		
US 6350456	B1	20020226	(200220)		
ZA 2000005505	A	20020227	(200223)		115
JP 2002510494	W	20020409	(200227)		115
MX 2000009803	A1	20010901	(200239)		
AU 753995	B	20021031	(200282)		

NZ 507378 A 20021220 (200309)
US 6544522 B1 20030408 (200327)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9951748	A2		WO 1999-US7717	19990407
AU 9934817	A		AU 1999-34817	19990407
EP 1068329	A2		EP 1999-916513	19990407
			WO 1999-US7717	19990407
NO 2000005050	A		WO 1999-US7717	19990407
			NO 2000-5050	20001006
CZ 2000003652	A3		WO 1999-US7717	19990407
			CZ 2000-3652	19990407
HU 2001001521	A2		WO 1999-US7717	19990407
			HU 2001-1521	19990407
BR 9909472	A		BR 1999-9472	19990407
			WO 1999-US7717	19990407
CN 1304451	A		CN 1999-807077	19990407
KR 2001071138	A		KR 2000-711196	20001007
US 6350456	B1	CIP of	US 1997-818112	19970313
		CIP of	US 1997-942578	19971001
		CIP of	US 1998-25197	19980218
			US 1998-56556	19980407
ZA 2000005505	A		ZA 2000-5505	19990407
JP 2002510494	W		WO 1999-US7717	19990407
			JP 2000-542460	19990407
MX 2000009803	A1		MX 2000-9803	20001006
AU 753995	B		AU 1999-34817	19990407
NZ 507378	A		NZ 1999-507378	19990407
			WO 1999-US7717	19990407
US 6544522	B1		US 1998-223040	19981230

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9934817	A	Based on	WO 9951748
EP 1068329	A2	Based on	WO 9951748
CZ 2000003652	A3	Based on	WO 9951748
HU 2001001521	A2	Based on	WO 9951748
BR 9909472	A	Based on	WO 9951748
JP 2002510494	W	Based on	WO 9951748
AU 753995	B	Previous Publ.	AU 9934817
		Based on	WO 9951748
NZ 507378	A	Based on	WO 9951748

PRIORITY APPLN. INFO: US 1998-223040 19981230; US 1998-56556 19980407; US 1997-818112 19970313; US 1997-942578 19971001; US 1998-25197 19980218

AB WO 9951748 A UPAB: 20030429
NOVELTY - Fusion **proteins** (I) containing at least two **Mycobacterium** tuberculosis antigens, are new.
DETAILED DESCRIPTION - The 11 new **proteins** are bi-, tri-, tetra- or penta-fusion **proteins**, and have the following M. tuberculosis antigens: TbH9-Tb38-1, TbH9-Ra35, DPV-MTI-MSL, TbH9-DPV-MTI, Ra12-TbH9-Ra35, Erd14-DPV-MTI, TbRa3-38kD-Tb38-1, TbRa3-38kD-Tb38-1-DPEP, Erd14-DPV-MTI-MSL, DPV-MTI-MSL-MTCC1, Erd14-DPV-MTI-MSL-MTCC2, with fully defined sequences given in the specification (optionally containing conservative amino acid substitution(s)).

An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising a polynucleotide (II) that encodes (I).

ACTIVITY - Antibacterial; tuberculostatic.

C57BL/6 mice were immunized with fusion **proteins** Ra12-TbH9-Ra35 or Erd14-DPV-MTI DNA, and exhibited a significant protection against tuberculosis upon a subsequent aerosol challenge of live M. tuberculosis bacteria.

MECHANISM OF ACTION - Vaccine.

Tri-fusion **protein** RA12-TbH9-Ra35 was injected into the footpads of mice for immunization, and a second immunization given after three weeks. A strong T cell proliferation response was seen.

USE - The new fusion **proteins** and (II) are useful as vaccines for preventing **tuberculosis** (claimed), for **diagnosis** (via in vitro **assays** or intradermal skin **tests** for detection of anti-M. tuberculosis antibodies), monitoring of disease progression, and treatment of tuberculosis.

(II) is useful for generating recombinant (I) in vitro, and anti-M. tuberculosis antibodies generated by (I) are useful for detecting target antigens in vivo and in vitro.

ADVANTAGE - Current tuberculosis vaccine Bacillus Calmette-Guerin (BCG)) is not considered safe for general vaccination in the United States, and has problems with **diagnosis** of **tuberculosis** due to its sensitivity and specificity.

The new fusion **proteins** are more effective immunogens than mixtures of the individual **protein** components. Fusion **protein** Ra12-TbH9-Ra35 or its individual components were administered to guinea pigs, and subsequently challenged with M. tuberculosis. When formulated in adjuvant SBAS2, over 75% of animals administered with the fusion had survived 11 weeks post challenge, compared to less than 25% of animals administered with the individual components.

Dwg.0/0

L80 ANSWER 48 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-551043 [46] WPIDS
DOC. NO. NON-CPI: N1999-407767
DOC. NO. CPI: C1999-160738
TITLE: New **mycobacterial** polypeptide produced in lactic acid bacteria, useful in **tuberculosis** **diagnosis** and vaccines.
DERWENT CLASS: B04 C06 D16 S03
INVENTOR(S): FOLKERSEN, J R; JENSEN, C L; FOLKERSEN, J
PATENT ASSIGNEE(S): (STAT-N) STATENS SERUMINSTITUT; (STAT-N) STATENS SERUM INST
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9945119	A2	19990910	(199946)*	EN	76
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9926119	A	19990920	(200007)		
EP 1058731	A2	20001213	(200066)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002505106 W		20020219	(200216)		74
AU 749672	B	20020704	(200255)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9945119	A2	WO 1999-DK109	19990305
AU 9926119	A	AU 1999-26119	19990305
EP 1058731	A2	EP 1999-906089	19990305
		WO 1999-DK109	19990305
JP 2002505106	W	WO 1999-DK109	19990305
		JP 2000-534650	19990305
AU 749672	B	AU 1999-26119	19990305

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9926119	A	Based on	WO 9945119
EP 1058731	A2	Based on	WO 9945119
JP 2002505106	W	Based on	WO 9945119
AU 749672	B	Previous Publ.	AU 9926119
		Based on	WO 9945119

PRIORITY APPLN. INFO: US 1998-77105P 19980306; DK 1998-306 19980306

AB WO 9945119 A UPAB: 19991110

NOVELTY - A bioreactive polypeptide (or immunologically equivalent analog) produced in lactic acid bacteria which reacts with lymphoid cells primed with **Mycobacterium** tuberculosis complex **mycobacteria** (M. tuberculosis, M. africanum or M. bovis) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) bioreactive polypeptides (or immunological equivalents) derived from **mycobacterium** other than those of the M. tuberculosis complex, with which lymphoid cells primed with **mycobacteria** can react;

(2) ESAT-6 homopolymer polypeptides comprising at least two copies of ESAT-6 optionally linked with a linker sequence and optionally with an N-terminal leader sequence;

(3) vaccines for immunizing animals (including humans) against tuberculosis, comprising at least one copy of ESAT-6 homopolymer-encoding sequence, allowing promotion of ESAT-6 homopolymer expression in cells; and

(4) vaccines of (3) in which coding sequence is incorporated into the genome of a non-pathogenic microorganism (e.g. M. bovis BCG strain Danish 1331), allowing it to express, and optionally secrete, polypeptide.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

The delayed type hypersensitivity (DTH) reaction protocol is as follows:

(a) Dunkin Hartley guinea pigs are infected intravenously with M. tuberculosis strain H37Rv (0.5 x 105 colony forming units (cfu));

(b) 4 weeks later, animals are injected intradermally with 100 mu l partially purified polypeptide (20 mu g/ml in phosphate buffered saline (PBS), 0.005 % polysorbate and 0.01 % chinisol);

(c) inflammatory reaction size at injection sites is measured by ruler at day 2, 5 mm or greater diameter indicating a positive reaction.

The bioreactive polypeptide elicits a positive DTH reaction in at least 10 % of guinea pigs infected with virulent M. tuberculosis complex **mycobacteria**.

USE - The polypeptide and ESAT-6 polypeptide are useful in

compositions (optionally with an adjuvant; claimed) for **diagnosis** of and vaccination against **tuberculosis** caused by M. **tuberculosis** complex **mycobacteria**. For example, the ESAT-6 polypeptide can be used to diagnose ongoing/previous sensitization with these bacteria by detecting cytokine release when contacting blood samples with the polypeptide. The polypeptide of (1) may be used in diagnostic compositions and vaccines (optionally with an adjuvant; claimed) for **mycobacteria** other than of the M. tuberculosis complex, e.g. M. avium which infects poultry and occasionally humans, M. leprae etc.; they are especially useful when they do not react with lymphoid cells previously primed with M. tuberculosis complex **mycobacteria**, and so do not give rise to a diagnostic reaction in individuals infected with these bacteria. The polypeptides may also be used in in vitro diagnostic **tests** e.g. stimulation of IFN- gamma release from lymphocytes (all claimed).

ADVANTAGE - The polypeptide has similar or higher bioreactivity as currently used tuberculin reagent in the standard DTH skin **test** for tuberculosis, but may have greater specificity, being better able to discriminate between lymphoid cells primed from tuberculosis and from previous vaccination.

Dwg.0/5

L80 ANSWER 49 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-527409 [44] WPIDS
CROSS REFERENCE: 1997-192903 [17]; 1998-251292 [22]; 1998-261042 [23]; 1999-601610 [51]; 2002-171134 [22]
DOC. NO. CPI: C1999-154908
TITLE: New antigens from **Mycobacterium** tuberculosis useful in diagnostic skin **tests** and protective or therapeutic vaccines or compositions.
DERWENT CLASS: B04 D16
INVENTOR(S): CAMPOS-NETO, A; DILLON, D C; HENDRICKSON, R C; HOUGHTON, R; LODES, M J; REED, S G; SKEIKY, Y A W; TWARDZIK, D R; VEDVICK, T S
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9942076	A2	19990826	(199944)*	EN	298
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9927663	A	19990906	(200003)		
ZA 9901303	A	20000531	(200032)		301
EP 1071451	A2	20010131	(200108)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002503683 W		20020205	(200212)		690

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9942076	A2	WO 1999-US3268	19990217
AU 9927663	A	AU 1999-27663	19990217
ZA 9901303	A	ZA 1999-1303	19990218
EP 1071451	A2	EP 1999-908169	19990217

	WO 1999-US3268	19990217
JP 2002503683 W	WO 1999-US3268	19990217
	JP 2000-532093	19990217

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9927663	A	Based on	WO 9942076
EP 1071451	A2	Based on	WO 9942076
JP 2002503683 W		Based on	WO 9942076

PRIORITY APPLN. INFO: US 1998-72967 19980505; US 1998-25197 19980218

AB WO 9942076 A UPAB: 20021220

NOVELTY - Polypeptide (I) comprises an immunogenic part of a **Mycobacterium** tuberculosis antigen (Ag), or its variant with only conservative substitutions and/or modifications, having specified N-terminal sequences or encoded by specific DNA sequences (II).

DETAILED DESCRIPTION - Soluble Ag have one of the N-terminal sequences (S120)-(S128) or (S136), other Ag have N-terminal sequences (S129) or (S137).

DPVDAVINTTCNYGQVVAAL (S120);
AVESGMLALGTPAPS (S121);
AAMLPRTGDGPLEAAKEGR (S122);
YYWCPGQPFDPAWGP (S123);
DIGSESTEDQQXAV (S124);
AEESISTXEXIVP (S125);
DPEPAPPVPTTAASPPS (S126);
APKTYXEELKGTDTG (S127);
DPASAPDVPTAAQLTSLLNSLADPNVSFAN (S128);
APESGAGLGGTVQAG (S136);
APPDPHQXDMTKGYYPGGRRXF (S129);
XYIAYXTTAGIVPGKINVHLV (S137);
each X = any amino acid.

Alternatively, soluble Ag are encoded by 27 DNA sequences and other Ag by 75 sequences, or their complements, or by sequences, or their complements, that hybridize under moderately stringent conditions (all sequences reproduced).

INDEPENDENT CLAIMS are also included for the following:
(1) DNA (II) encoding (I);
(2) expression vectors containing (II);
(3) host cells transformed with this vector;
(4) pharmaceutical composition containing (I) or (II) and a carrier;
(5) similar composition containing at least one of about 65 specified DNA sequences (IIa) given in the specification;
(6) vaccine containing at least one (I) plus a non-specific immune enhancer (A);
(7) vaccine containing polypeptides (Ia) with N-terminal sequences (S134) or (S135), and (A);
(8) vaccine containing a polypeptide (Ib) encoded by (IIa), their complements or sequences that hybridize to them, plus (A);
(9) vaccines containing (II) or (IIa) plus (A);
(10) fusion **protein** (FP1) of two or more (I);
(11) fusion **protein** (FP2) of at least one (I) plus ESAT-6 or the 38 kD M. tuberculosis antigen;
(12) pharmaceutical composition containing FP1 or 2 and carrier;
(13) vaccine containing FP1 or 2 plus (A); and
(14) diagnostic kit, for detecting tuberculosis in a skin test, containing (I), (Ia), (II), (IIa) or FP1 or 2.

XDSEKSATIKVTDAS (S134);

AGDTXIYIVGNLTAD (S135).
ACTIVITY - Antibacterial; Tuberculostatic.
MECHANISM OF ACTION - Vaccine.
USE - (I), DNA (II) encoding them, derived fusion proteins and other polypeptides (Ia), or DNA (IIa) encoding them, are used in pharmaceutical compositions or vaccines to generate a protective or therapeutic immune response to M. tuberculosis and as reagents in skin tests for diagnosis of tuberculosis.
ADVANTAGE - Ag can induce proliferation of, or cytokine secretion by, T, B or natural killer cells and/or macrophages in tuberculosis-immune subjects.
Dwg.0/12

L80 ANSWER 50 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-312870 [26] WPIDS
DOC. NO. CPI: C1999-092334
TITLE: Method of detecting mycothiol and its precursors.
DERWENT CLASS: B03 B04 D16
INVENTOR(S): ANGERBERG, S J; DAVIS, C E; FAHEY, R C; NEWTON, G L; UNSON, M M D
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9921580	A1	19990506	(199926)*	EN	110
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9911988	A	19990517	(199939)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9921580	A1	WO 1998-US22577	19981023
AU 9911988	A	AU 1999-11988	19981023

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9911988	A	Based on	WO 9921580

PRIORITY APPLN. INFO: US 1997-63620P 19971027
AB WO 9921580 A UPAB: 20011203
NOVELTY - Detecting mycothiol (MSH), 1-D-myo-inositol-2-(N-acetyl-L-cysteinyl)amido-2-deoxy- alpha -D-glucopyranosideor its precursors (MSHa) comprising:
(i) a reaction with a reagent (I) for fluorescent labeling of thiol or amino groups, then detecting the product formed; or
(ii) biotinylation of MSH or MSHa, reaction with an antibody (Ab) against MSH or MSHa and detecting the complex formed with a reagent (II); is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) detecting a member of the taxa Actinomycetes by detecting MSH or

MSHa;
(2) an antibody (Ab) that binds to MSH or MSHa;
(3) diagnosis of Actinomycetes-related disease, or susceptibility, by detecting MSH or MSHa;
(4) identifying a sample with altered production of MSH or MSHa;
(5) detecting MSH and MSHa in a bacterial colony; and
(6) a kit for detecting the presence of MSH or MSHa.
ACTIVITY - Antimicrobial.
MECHANISM OF ACTION - None given.
USE - Detection of MSH or MSHa is particularly used to detect Actinomycetes, specifically **Mycobacterium tuberculosis** infections. Antibodies are used as reagents for **diagnosis** and monitoring infections and as immunotherapeutic agents.
ADVANTAGE - Production of MSH is specific to Actinomycetes. The use of antibodies provides an **assay** for MSH that is at least 10 times more sensitive than known procedures.

L80 ANSWER 51 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-132249 [11] WPIDS
DOC. NO. NON-CPI: N1999-096270
DOC. NO. CPI: C1999-038780
TITLE: New nucleic acid containing regulator and LHP gene of **Mycobacterium tuberculosis** - useful in vaccines, for **diagnosis**, and for expression of heterologous **proteins**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): ANDERSEN, P; BERTHET, F; GICQUEL, B; RASMUSSEN, P B; ANDERSON, P
PATENT ASSIGNEE(S): (INSP) INST PASTEUR; (STAT-N) STATENS SERUM INST
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9904005	A1	19990128	(199911)*	EN	88
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9881238	A	19990210	(199925)		
EP 1003870	A1	20000531	(200031)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6436409	B1	20020820	(200257)		
US 2003092899	A1	20030515	(200335)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9904005	A1		WO 1998-IB1091	19980716
AU 9881238	A		AU 1998-81238	19980716
EP 1003870	A1		EP 1998-930967	19980716
			WO 1998-IB1091	19980716
US 6436409	B1	Provisional	US 1997-52631P	19970716
			US 1998-116492	19980716
US 2003092899	A1	Provisional	US 1997-52631P	19970716
		Div ex	US 1998-116492	19980716
			US 2002-140045	20020508

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9881238	A	Based on	WO 9904005
EP 1003870	A1	Based on	WO 9904005
US 2003092899	A1	Div ex	US 6436409

PRIORITY APPLN. INFO: US 1997-52631P 19970716; US 1998-116492 19980716; US 2002-140045 20020508

AB WO 9904005 A UPAB: 19990324
New polynucleotide (I) is: (a) a sequence of approximately 1.3 kb (S1); (b) is the 1-524 (S2), 1-481 (S3) or 525-826 (S4) bp fragment of (S1), also a biologically active derivative of (S2) or (S3); (c) contains at least 12 consecutive nucleotides (nt) from (S2)-(S4); (d) is the complement of (S2)-(S4); or (e) hybridises under stringent conditions to (S2)-(S4).

Also new are: (A) polynucleotides (Ia) comprising (S2), (S3) or their active derivatives fused to a sequence (II) encoding a polypeptide (III); (B) recombinant vectors containing (I) or (Ia); (C) recombinant host cells containing (I), (Ia) or the vector of (B); (D) polypeptide (IIIa) expressed by these host cells, their oligomers or antigenic fragments; (E) mono- or poly-clonal antibodies (Ab) specific for (IIIa) or their oligomers; and (F) the (1)-derived probes or primers (P14), (P15), and (P16), which can be used in pairs P14/P15, or P14/P16. 5'-CTGCAGCAGGTGACGTCGTTG (P14), 5'-CCGGGTGGCCGGGAAGTCTGTGT (P15), 5'-ACTACTTTCTCTTTCTACCTTCC (P16).

USE - (IIIa) and their oligomers are used: (a) as immunogens and vaccines, to protect against bacteria of the **Mycobacterium** tuberculosis (M.t.) complex in humans or animals (the vaccines may include other immunogenic **proteins** of M.t. or their fragments, specifically ESAT-6); and (b) for diagnosing M.t. infection by detection of specific antibodies (claimed).

Also the cells of (C) can be used as vaccines. Ab are used diagnostically to detect M.t., particularly in serum, and (I) or its fragments can be used to detect the M.t. complex or M.bovis by standard hybridisation or amplification **assays** (claimed).

Also the regulatory region present in (S1) may be used to express almost any heterologous **protein** in **mycobacteria**, particularly as a fusion with polyhistidine.

ADVANTAGE - The two **proteins** encoded in (S1), LHP and ESAT-6, are expected to provide a synergistic increase in ability to induce a protective immune response.

Dwg.0/13

L80 ANSWER 52 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-085791 [07] WPIDS
DOC. NO. NON-CPI: N2000-067266
DOC. NO. CPI: C2000-023946
TITLE: Identifying compounds that regulate the growth of **Mycobacterium** tuberculosis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BISHAI, W R; DEMAIO, J; YOUNG, D B; ZHANG, Y
PATENT ASSIGNEE(S): (UYJO) UNIV JOHNS HOPKINS
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6004764	A	19991221	(200007)*		27

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6004764	A	CIP of	US 1996-622352	19960327
		CIP of	US 1996-622353	19960327
			US 1997-826390	19970409

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6004764	A	CIP of	US 5700925
		CIP of	US 5824546

PRIORITY APPLN. INFO: US 1997-826390 19970409; US 1996-622352 19960327; US 1996-622353 19960327

AB US 6004764 A UPAB: 20000209
NOVELTY - Methods ((I) and (II)) for identifying compounds that regulate the growth of **Mycobacterium** tuberculosis by modulating binding between the **peptides** sigF and orfX, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a method (I) of identifying compounds that regulate the binding of M. tuberculosis sigF to M. tuberculosis orfX, comprising:
(i) incubating M. tuberculosis sigF immobilized on a solid support with a **test** compound and M. tuberculosis orfX; and
(ii) determining the amount of sigF bound to orfX (a desirable **test** compound is one that either increases or decreases the binding of orfX to sigF); and
(2) a method (II) of identifying compounds that regulate the binding of M. tuberculosis orfX to M. tuberculosis sigF, comprising:
(i) incubating M. tuberculosis orfX immobilized on a solid support with a **test** compound and M. tuberculosis sigF; and
(ii) determining the amount of sigF bound to orfX (a desirable **test** compound is one that either increases or decreases the binding of orfX to sigF).
USE - (I) and (II) may be used to select compounds that may be used to regulate the growth and dormancy of M. **tuberculosis**, and therefore be used in the **diagnosis**, prevention and treatment of latent **tuberculosis**.
Dwg.0/4

L80 ANSWER 53 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-110232 [10] WPIDS
DOC. NO. CPI: C1998-036199
TITLE: Nucleic acid encoding **mycobacterial protein** involved in cell binding and entry - used for diagnosis of **Mycobacterium** infection and in vaccines for humans or animals.
DERWENT CLASS: B04 C06 C07 D16
INVENTOR(S): ANAND, N N; KLEIN, M H
PATENT ASSIGNEE(S): (CONN-N) CONNAUGHT LAB LTD; (AVET) AVENTIS PASTEUR LTD
COUNTRY COUNT: 78
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9801559	A1	19980115	(199810)*	EN	107

RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU ZW

AU 9733318 A 19980202 (199826)
EP 938561 A1 19990901 (199940) EN
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI
MX 9900497 A1 19990401 (200055)
NZ 333988 A 20001027 (200062)
JP 2000516449 W 20001212 (200101) 111
AU 731979 B 20010412 (200128)
BR 9712968 A 20020205 (200213)
US 6444444 B1 20020903 (200260)
US 2003017494 A1 20030123 (200310)
US 2003018178 A1 20030123 (200310)
US 2003023056 A1 20030130 (200311)
US 2003088082 A1 20030508 (200337)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9801559	A1		WO 1997-CA484	19970709
AU 9733318	A		AU 1997-33318	19970709
EP 938561	A1		EP 1997-929065	19970709
			WO 1997-CA484	19970709
MX 9900497	A1		MX 1999-497	19990111
NZ 333988	A		NZ 1997-333988	19970709
			WO 1997-CA484	19970709
JP 2000516449	W		WO 1997-CA484	19970709
			JP 1998-504612	19970709
AU 731979	B		AU 1997-33318	19970709
BR 9712968	A		BR 1997-12968	19970709
			WO 1997-CA484	19970709
US 6444444	B1		US 1996-677970	19960710
US 2003017494	A1	Cont of	US 1996-677970	19960710
			US 2002-176667	20020624
US 2003018178	A1	Div ex	US 1996-677970	19960710
			US 2002-176687	20020624
US 2003023056	A1	Cont of	US 1996-677970	19960710
			US 2002-176640	20020624
US 2003088082	A1	Cont of	US 1996-677970	19960710
			US 2002-178495	20020625

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9733318	A	Based on	WO 9801559
EP 938561	A1	Based on	WO 9801559
NZ 333988	A	Based on	WO 9801559
JP 2000516449	W	Based on	WO 9801559
AU 731979	B	Previous Publ.	AU 9733318
		Based on	WO 9801559
BR 9712968	A	Based on	WO 9801559
US 2003017494	A1	Cont of	US 6444444
US 2003018178	A1	Div ex	US 6444444
US 2003023056	A1	Cont of	US 6444444
US 2003088082	A1	Cont of	US 6444444

PRIORITY APPLN. INFO: US 1996-677970 19960710; US 2002-176667 20020624; US 2002-176687 20020624; US 2002-176640 20020624; US 2002-178495 20020625

AB WO 9801559 A UPAB: 19980323
Isolated nucleic acid (I) encoding a **mycobacterial protein** (II) which is associated with cell binding and entry and has a molecular weight of about 45-60 kDa, and its fragments, are new.
Also claimed are:
(1) vectors containing (I);
(2) cells transformed with this vector;
(3) (II) and its fragments, including recombinant **protein** produced by the cells of (3), and
(4) 9 specified oligonucleotide primers.
USE - (I) is used in hybridisation **tests** to detect nucleic acid encoding (II) in a sample (specifically for **diagnosis** of **Mycobacterium tuberculosis** infection), while its fragments are used in polymerase chain reaction (PCR) to detect **Mycobacterium** in tissues and body fluids, also for isolating related genes.
Cells of (2) are used to make recombinant (II). (I) and (recombinant) (II), or their active fragments, are used in immunogenic compositions to generate an immune response, i.e. to protect humans and animals (specifically cattle) against **mycobacterial** infections.
Vaccines containing (II) are administered by subcutaneous, intradermal or intramuscular injection, or orally or nasally to mucosal surfaces. (I) may be delivered directly or in usual vectors, e.g. Salmonella or viruses.
Dwg.12/14

L80 ANSWER 54 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1997-549750 [50] WPIDS
DOC. NO. CPI: C1997-175389
TITLE: New DNA and related **proteins** or RNA derived from M. **tuberculosis** - used for **diagnosis** of **mycobacterial** infections, monitoring vaccination and development of anti-**mycobacterial** agents.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): ESPITIA, C; HONISCH, C; MORENO, C; SINGH, M
PATENT ASSIGNEE(S): (GBFB) GES BIOTECHNOLOGISCHE FORSCHUNG MBH; (GBFB) GBF GES BIOTECH FORSCHUNG GMBH
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9741252	A2	19971106	(199750)*	EN	55
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP US					
WO 9741252	A3	19971211	(199816)		
EP 907751	A2	19990414	(199919)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE					
JP 2000509981 W		20000808	(200043)		60

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9741252	A2	WO 1997-EP1973	19970418
WO 9741252	A3	WO 1997-EP1973	19970418
EP 907751	A2	EP 1997-921666	19970418

	WO 1997-EP1973	19970418
JP 2000509981 W	JP 1997-538524	19970418
	WO 1997-EP1973	19970418

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 907751	A2	Based on	WO 9741252
JP 2000509981 W		Based on	WO 9741252

PRIORITY APPLN. INFO: DE 1996-19617184 19960429

AB WO 9741252 A UPAB: 19980112
New DNA (A): (a) has one of 3 sequences (reproduced) of 3946 bp (I), 2653 bp (VI) or 440 bp (IX), optionally with one or more codons replaced by codons for the same amino acid (aa); (b) sequences complementary to (a); (c) if single-stranded is hybridisable to (a) or (b); (d) if double-stranded is an (a)-(b) duplex or has individual strands hybridisable with this duplex, or (e) is a fragment of any of (a)-(d).
USE - (A)-(C) are all useful for diagnosing tuberculosis and other **mycobacterial** infections, in humans or animals. (A) can also be used to identify **mycobacteria** in (clinical) samples (by hybridisation or amplification), including differentiation between strains, while (A) and (C) can be used (i) for epidemiological studies; (ii) for monitoring vaccination (e.g. serological or skin **tests**) or (iii) in development of anti-**mycobacterial** drugs and vaccines.
Dwg.0/16

L80 ANSWER 55 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-239918 [25] WPIDS
CROSS REFERENCE: 1994-043334 [06]
DOC. NO. NON-CPI: N1996-200843
DOC. NO. CPI: C1996-076627
TITLE: Coated support for **tuberculosis** or leprosy **diagnosis** - contains synthetic pseudo-cord factor glyco-lipid as antigen, used in rapid, reliable dot-blot **assay test**.
DERWENT CLASS: A96 B04 C07 D16 S03
INVENTOR(S): HANDZEL, V; LASZLO, A; VERA-CABRERA, L
PATENT ASSIGNEE(S): (LASZ-I) LASZLO A; (CNDG) CANADA MIN HEALTH
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2157522	A	19960303	(199625)*		36
US 5597735	A	19970128	(199710)		15

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
CA 2157522	A		CA 1995-2157522	19950901
US 5597735	A	CIP of	US 1992-881193	19920511
			US 1994-300268	19940902

FILING DETAILS:

PATENT NO	KIND	PATENT NO

US 5597735 A CIP of US 5344759

PRIORITY APPLN. INFO: US 1994-300268 19940902; US 1992-881193 19920511

AB CA 2157522 A UPAB: 19970313

A spot **test** kit for serodiagnosis of tuberculosis in a human or animal suspected of being exposed to **Mycobacterium** tuberculosis comprises: at least one tube for collecting a blood sample; **protein** A-colloidal gold conjugate; a rabbit anti-human immunoglobulin; instructions for carrying out the **test** procedure, and a strip of **test** paper (pref. nitrocellulose paper) coated with a synthetic pseudo cord factor-like glycolipid of formula (I), the amt. of (I) in the coating pref. being ca. 1 mu g. Also claimed is a coated support suitable for **assays** for detecting tuberculosis and leprosy in humans and animals, comprising a solid support having an immobilised coating layer of (I).

USE - (I) is useful as antigen in a spot **test** (dot-blot **assay**) for tuberculosis or leprosy.

ADVANTAGE - The **assay** is reliable, simple and rapid. (I) has high serodiagnostic discriminating activity (sensitivity and specificity) for **Mycobacterium** tuberculosis and M. leprae, and is stable at ambient temp. The **assay** has almost equal sensitivity and specificity to a beta -galactosidase ELISA **test**, and can be carried out in places where ELISA appts. is not available (e.g. developing countries).

Dwg.0/4

L80 ANSWER 56 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1994-026154 [03] WPIDS
DOC. NO. CPI: C1994-012090
TITLE: Compsn. contg. recombinant nucleic acid encoding e.g. antigenic ATPase - useful in vaccines against **mycobacteria** or other diseases e.g. HIV, cholera, etc. and as diagnostic agents.
DERWENT CLASS: B04 D16
INVENTOR(S): KAPOOR, A; MUNSHI, A
PATENT ASSIGNEE(S): (KAPO-I) KAPOOR A; (MUNS-I) MUNSHI A
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9400493	A1	19940106	(199403)*	EN	49
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9346511	A	19940124	(199420)		
US 5330754	A	19940719	(199428)		32
EP 649435	A1	19950426	(199521)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 07508649	W	19950928	(199547)		13
US 5559011	A	19960924	(199644)		30
EP 649435	A4	19961227	(199721)		
AU 689075	B	19980326	(199826)		
US 5770719	A	19980623	(199832)		
US 6045798	A	20000404	(200024)		
US 2003099673	A1	20030529	(200337)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 9400493	A1		WO 1993-US6080	19930628
AU 9346511	A		AU 1993-46511	19930628
US 5330754	A		US 1992-906395	19920629
EP 649435	A1		EP 1993-916768	19930628
			WO 1993-US6080	19930628
JP 07508649	W		WO 1993-US6080	19930628
			JP 1994-502594	19930628
US 5559011	A	Div ex	US 1992-906395	19920629
			US 1994-192632	19940207
EP 649435	A4		EP 1993-916768	
AU 689075	B		AU 1993-46511	19930628
US 5770719	A	Div ex	US 1992-906395	19920629
		Div ex	US 1994-192632	19940207
			US 1996-710676	19960923
US 6045798	A	Div ex	US 1992-906395	19920629
		Div ex	US 1994-192632	19940207
		Div ex	US 1996-710676	19960923
			US 1998-99902	19980618
US 2003099673	A1	Div ex	US 1992-906395	19920629
		Div ex	US 1994-192632	19940207
		Div ex	US 1996-710676	19960923
		Cont of	US 1998-99902	19980618
			US 1999-432820	19991102

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9346511	A	Based on	WO 9400493
EP 649435	A1	Based on	WO 9400493
JP 07508649	W	Based on	WO 9400493
US 5559011	A	Div ex	US 5330754
AU 689075	B	Previous Publ.	AU 9346511
		Based on	WO 9400493
US 5770719	A	Div ex	US 5330754
		Div ex	US 5559011
US 6045798	A	Div ex	US 5330754
		Div ex	US 5559011
		Div ex	US 5770719
US 2003099673	A1	Div ex	US 5330754
		Div ex	US 5559011
		Div ex	US 5770719
		Cont of	US 6045798

PRIORITY APPLN. INFO: US 1992-906395 19920629; US 1994-192632 19940207; US 1996-710676 19960923; US 1998-99902 19980618; US 1999-432820 19991102

AB WO 9400493 A UPAB: 19940303

Compsn. comprises recombinant nucleic acid (I) encoding (part of) a membrane-associated polypeptide (II) of a **mycobacterium** which can induce an immune response that is detectable by (part of) (II).

Also new are (1) compsns. contg. (II) and (2) nucleic acid (Ia) comprising a promoter sequence from an ion-motive ATPase (IIa) of a **mycobacterium**.

Pref. (I) is derived from the **mycobacterium** species tuberculosis, leprae, africanum, microti, avium, intracellular. scrofulaceum or bovis, esp. M. bovis BCG. (IIa) is esp. of mol.wt. 79 kD and is encoded by a 3250bp sequence reproduced in the specification together with the 761 aminoacid sequence of the **protein**.

USE/ADVANTAGE - (II), or (I) expressing it in a recombinant viral or bacterial vehicle, are useful in vaccines and (not claimed) as diagnostic

reagents (e.g. (I) in hybridisation **tests** and (II) to detect antibodies). These vaccines can protect against **Mycobacteria** or (when non-**mycobacterial** antigens are expressed on the surface of culturable **mycobacterial** strains) against other diseases (e.g. aphthous fever, HIV or cholera). (Ia) is useful for expressing homologous or heterologous antigens in **mycobacteria** or other organisms such as E. coli.
Dwg.0/0

L80 ANSWER 57 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1994-043334 [06] WPIDS
CROSS REFERENCE: 1996-239918 [25]
DOC. NO. NON-CPI: N1994-034355
DOC. NO. CPI: C1994-019369
TITLE: **Tuberculosis** and leprosy **diagnosis** in animals and humans - using readily prepd. glyco-lipid antigens to bind antibodies in their sera.
DERWENT CLASS: B03 B04 D16 S03
INVENTOR(S): HANDZEL, V; LASZLO, A
PATENT ASSIGNEE(S): (LASZ-I) LASZLO A; (CNDG) CANADA MIN HEALTH
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2092637	A	19931112	(199406)*		25
US 5344759	A	19940906	(199435)		15

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2092637	A	CA 1993-2092637	19930312
US 5344759	A	US 1992-881193	19920511

PRIORITY APPLN. INFO: US 1992-881193 19920511
AB CA 2092637 A UPAB: 19970313
Testing for tuberculosis and leprosy in animals and humans comprises **assay** of their sera using a pseudo cord factor like glycolipid antigen or formulae (I) or (II) to bind antibodies in the sera, (R = 15-18C alkyl; and Oc = octadecyl).
USE/ADVANTAGE - (I) and (II) provide reliable and specific **diagnosis** of **tuberculosis** and leprosy, using an antigen/antibody binding reaction. For this purpose, they are pref. immobilised as a coating layer on a solid support. The support is either a plate provided with wells contg. the coating, for enzyme linked immunosorbent **assay** (ELISA); or a paper web, esp. as a strip, for spot **tests**. Either **assay** can be conveniently provided in the form of a kit with instructions explaining the **test** procedure; the ELISA kit comprising a coated multiple well microtitre plate, a conjugate, and substrate as detector; the spot **test** comprising culture tube(s), coated paper strip(s), and **protein** A colloidal gold conjugate, which is commercially available, in place of conjugate and substrate. (I) and (II) provide diagnosis in a single **test** for these widespread diseases, unlike prior art **tests** beset with problems of false positives, necessitating further **tests**, or use of a bacterial antigen of limited availability. By contrast, (I) and (II) are easily synthesised from trehalose by known methods, and have high serodiagnostic discriminating activity for both M. tuberculosis and M. leprae. They are

also reasonably stable under ambient conditions, and can be stored and distributed without refrigeration.
Dwg.0/2

L80 ANSWER 58 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1992-096598 [12] WPIDS
DOC. NO. CPI: C1992-044816
TITLE: New nucleotide sequences - produce antibodies reacting with M. tuberculosis used as hybridisation probes and as vaccines against tuberculosis.
DERWENT CLASS: B04 D16
INVENTOR(S): PATARROYO, M E; PATARROYOME
PATENT ASSIGNEE(S): (PATA-I) PATARROYO M E
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9203158	A	19920305	(199212)*		29
RW: AT CH DE DK ES GB GR LU NL SE					
W: AU CA JP KR					
AU 9185266	A	19920317	(199226)		
ZA 9106431	A	19920527	(199228)		31
US 5169940	A	19921208	(199252)		7
US 5171839	A	19921215	(199301)		7
NZ 239490	A	19930225	(199312)		
EP 550500	A1	19930714	(199328)	EN	29
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
US 5254459	A	19931019	(199343)		7
JP 05509233	W	19931222	(199405)		15
EP 550500	A4	19931013	(199527)		
PH 28499	A	19941011	(199840)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9203158	A		WO 1991-US5933	19910819
AU 9185266	A		AU 1991-85266	19910819
			WO 1991-US5933	19910819
ZA 9106431	A		ZA 1991-6431	19910814
US 5169940	A	Div ex	US 1990-572171	19900823
			US 1992-833932	19920211
US 5171839	A		US 1990-572171	19900823
NZ 239490	A		NZ 1991-239490	19910820
EP 550500	A1		EP 1991-916365	19910819
			WO 1991-US5933	19910819
US 5254459	A	Div ex	US 1990-572171	19900823
			US 1992-940468	19920904
JP 05509233	W		JP 1991-515653	19910819
			WO 1991-US5933	19910819
EP 550500	A4		EP 1991-916365	
PH 28499	A		PH 1991-42984	19910822

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9185266	A	Based on	WO 9203158
EP 550500	A1	Based on	WO 9203158
US 5254459	A	Div ex	US 5171839

JP 05509233 W Based on WO 9203158

PRIORITY APPLN. INFO: US 1990-572171 19900823
AB WO 9203158 A UPAB: 19931006
An oligonucleotide of specified 411 aminoacid sequence is new.
Also claimed are: (1) an oligonucleotide complementary to (I); (2) a compound, PT1, of formula: 5'CAACGCGCCGTGCCTGG 3' (II); (3) a compound, PT2, of formula 5'CCCCCCACGGCACC CG 3' (III); (4) a **protein** encoded a specified 134 aminoacid sequence.
USE - (I) or fragments is useful in a diagnostic or taxonomic typification system for **assaying** for the presence of M.tuberculosis in a sample of body fluids or body tissues contg. antibodies (Abs) or cells.
0/0

L80 ANSWER 59 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1990-171668 [23] WPIDS
DOC. NO. CPI: C1990-074831
TITLE: **Mycobacterial** antigen A60 - useful for vaccination against **tuberculosis** and **diagnosis** of prior **mycobacterial** infection.
DERWENT CLASS: B04 D16
INVENTOR(S): MAES, R R
PATENT ASSIGNEE(S): (ANDA-N) ANDA BIOLOGICALS
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
BE 1002022	A	19900522	(199023)*		
US 4965192	A	19901023	(199045)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
BE 1002022	A	BE 1989-456	19890425
US 4965192	A	US 1988-187919	19880429

PRIORITY APPLN. INFO: US 1988-187919 19880429
AB BE 1002022 A UPAB: 19930928
A new interspecific **mycobacterial** antigen, called A60, comprises an immunochemically pure mixt. of a **protein** with a molecular wt. of at least 4 MD and polysaccharides with a molecular wt. of at least 1 MD, and is characterised as having the same 2-dimensional immunoelectrophoretic pptn. pattern as the A60 antigen of **Mycobacterium** bovis BCG strain.
USE/ADVANTAGE - A60 is useful for prodn. of vaccines against tuberculosis and related diseases, and as a diagnostic aid for detection of prior exposure to **mycobacterial** infections by means of a delayed-hypersensitivity skin **test**. A60 may be isolated in purer form than conventional tuberculins, and is cross-reactive with antibodies to a wide range of **Mycobacterium** spp., e.g. M. bovis, M. avium, M. paratuberculosis, M. xenopi and M. kansasii.
0/3

L80 ANSWER 60 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1988-235175 [33] WPIDS
DOC. NO. NON-CPI: N1988-178838

DOC. NO. CPI: C1988-105224
TITLE: Genes encoding **Mycobacterium tuberculosis protein** antigens - useful for developing reagents for **diagnosis**, prevention and treatment of **tuberculosis**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HUSSON, R N; NICK, T M; YOUNG, R A
PATENT ASSIGNEE(S): (WHED) WHITEHEAD INST BIOMEDICAL RES
COUNTRY COUNT: 12
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8805823	A	19880811	(198833)*	EN	84
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU JP					
AU 8815483	A	19880824	(198847)		
EP 345299	A	19891213	(198950)	EN	
R: DE FR GB IT					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8805823	A	WO 1988-US281	19880201
EP 345299	A	EP 1988-902999	19880201

PRIORITY APPLN. INFO: US 1987-10007 19870202
AB WO 8805823 A UPAB: 19941115
Isolated DNA encoding an immunogenic **protein** antigen of **Mycobacterium** tuberculosis is claimed. Pref. embodiments (also claimed) comprise DNA encoding a **protein** antigen (i) of mol. wt. 65kD, recognised by monoclonal antibody IT-31, C1.1, IIH9, IIC8, T2.3, Y1-2, SA2C or IT-13; (ii) of mol. wt. 19kD, recognised by monoclonal antibody IT-10, IT-12, IT-16 or IT-19; or (iii) of mol. wt. 71kD recognised by monoclonal antibody IT-11. For antigen (i), the DNA is a DNA insert of clone Y3141, Y3143, Y3150, Y3253 or Y3262 (also claimed). Nucleotide sequences of the novel DNA are provided. Also claimed are **proteins/peptides** encoded by the nucleotide sequences, being specifically the antigenic determinant unique to M. tuberculosis **protein**, the **peptide** recognised by helper T cells and that encoded by clone Y3150, DNA insert. Also claimed are isolated DNA encoding a **protein** of M.-africanum and -avium, both of mol. wt. 65kD.

USE/ADVANTAGE - Genes may be used to develop reagents used in the **diagnosis**, prevention and treatment of **tuberculosis**. Used, e.g. in the development of skin- and serodiagnostic-**tests** and vacines specific for tuberculos (methods and vaccine compsn. are claimed). Genes encoding **proteins** of the other **mycobacteria** may be similarly used in diseases which they cause.
Dwg.0/43

L80 ANSWER 61 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1987-264177 [37] WPIDS
DOC. NO. NON-CPI: N1987-197836
DOC. NO. CPI: C1987-111973
TITLE: In vitro **assay** for detecting cell-mediated immune responses - by incubating whole blood with specific antigen and detecting gamma interferon.
DERWENT CLASS: B04 C03 D16 J04 S03

INVENTOR(S): CORNER, L A; WOOD, P R; CORNER, A L; WOOD, R P
PATENT ASSIGNEE(S): (CSIR) COMMONWEALTH SCI & IND RES ORG; (WOOD-I) WOOD P R
COUNTRY COUNT: 16
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8705400	A	19870911	(198737)*	EN	27
RW: AT BE CH DE FR GB LU NL SE					
W: AU JP NO					
AU 8771659	A	19870928	(198749)		
JP 63502695	W	19881006	(198846)		
EP 296158	A	19881228	(198901)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
CA 1299099	C	19920421	(199221)		
EP 296158	B1	19920617	(199225)	EN	13
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 3779909	G	19920723	(199231)		
US 5334504	A	19940802	(199430)		6
EP 296158	A4	19891123	(199508)		
US 5494799	A	19960227	(199614)		6
JP 2642112	B2	19970820	(199738)		8

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 8705400	A		WO 1987-AU61	19870305
JP 63502695	W		JP 1987-501950	19870305
EP 296158	A		EP 1987-901300	19870305
CA 1299099	C		CA 1987-531267	19870305
EP 296158	B1		EP 1987-901300	19870305
			WO 1987-AU61	19870305
DE 3779909	G		DE 1987-3779909	19870305
			EP 1987-901300	19870305
			WO 1987-AU61	19870305
US 5334504	A	Cont of	US 1988-272805	19881104
		Cont of	US 1993-3662	19930112
			US 1993-124439	19930922
EP 296158	A4		EP 1987-901300	
US 5494799	A	Cont of	US 1988-272805	19881104
		Cont of	US 1993-3662	19930112
		Cont of	US 1993-124439	19930922
			US 1994-230373	19940420
JP 2642112	B2		JP 1987-501950	19870305
			WO 1987-AU61	19870305

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 296158	B1	Based on	WO 8705400
DE 3779909	G	Based on	EP 296158
		Based on	WO 8705400
US 5494799	A	Cont of	US 5334504
JP 2642112	B2	Previous Publ.	JP 63502695
		Based on	WO 8705400

PRIORITY APPLN. INFO: AU 1986-4893 19860306; AU 1987-71659 19860306
AB WO 8705400 A UPAB: 19930922

An in vitro method of detecting a cell-mediated immune response to a specific antigen in a human or animal comprises (a) incubating a whole blood sample from the human or animal with the specific antigen and (b) detecting the presence of gamma interferon (gamma IFN) released by sensitised lymphocytes in the whole blood sample to indicate a cell-mediated immune response to the specific antigen. Pref. the gamma IFN is detected using an emxyme-linked immunosorbent **assay** or a radioimmunoassay.

USE/ADVANTAGE - The **assay** is far simpler and faster than those previously described. A single blood sample provides sufficient material for **testing** a patient's responsiveness to a wide variety of antigens. The method is used esp. for detecting immune response to the M.bovis antigen, tuberculin purified **protein** deriv. (PPD) in whole blood samples from cattle. The **assay** does not compromise the immune status of animals as does the current in vivo tuberculin skin **test**. The **assay** can also be used in detecting cellular responses to e.g. M. leprae, M. tuberculosis, mumps, Candida, Brucella, histoplasmin, trichophyton, coccidioidin and malaria.
0/0

L80 ANSWER 62 OF 62 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1987-064844 [09] WPIDS
DOC. NO. CPI: C1987-027063
TITLE: Synthetic polypeptide(s) for detecting **Mycobacterial** infections - comprise amino acid sequency corresp. to **Mycobacterium** bovis BCG-a **protein** amino-terminal sequence.
DERWENT CLASS: B04
INVENTOR(S): HOUGHTEN, R A; MINDEN, P; SHINNICK, T M; HOUGHTEN, A R; SHINNICK, M
PATENT ASSIGNEE(S): (SCRI) SCRIPPS CLINIC & RES FOUND
COUNTRY COUNT: 5
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8701118	A	19870226	(198709)*	EN	61
AU 8662293	A	19870310	(198721)		
EP 233936	A	19870902	(198735)	EN	
US 4689397	A	19870825	(198736)		14
JP 63500524	W	19880225	(198814)		
US 4889800	A	19891226	(199008)		15
CA 1306582	C	19920818	(199239)		
EP 233936	B1	19930407	(199314)	EN	29
DE 3688246	G	19930513	(199320)		
EP 233936	A4	19891108	(199508)		
JP 07062030	B2	19950705	(199531)		15
JP 07300497	A	19951114	(199603)		1
JP 2573815	B2	19970122	(199708)		15

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WO 8701118	A	WO 1986-US1687	19860812
EP 233936	A	EP 1986-905514	19860812
US 4689397	A	US 1985-765048	19850812
JP 63500524	W	JP 1986-504608	19860812
US 4889800	A	US 1987-88146	19870821
CA 1306582	C	CA 1986-515743	19860812
EP 233936	B1	EP 1986-905514	19860812

			WO 1986-US1687	19860812
DE 3688246	G		DE 1986-3688246	19860812
			EP 1986-905514	19860812
			WO 1986-US1687	19860812
EP 233936	A4		EP 1986-905514	
JP 07062030	B2		JP 1986-504608	19860812
			WO 1986-US1687	19860812
JP 07300497	A	Div ex	JP 1986-504608	19860812
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JP 2573815	B2	Div ex	JP 1986-504608	19860812
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EP 233936	B1	Based on	WO 8701118
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Synthetic polypeptides contg. 13-40 amino acid residues and including the 13 residue sequence of formula (I), and synthetic multimers contg. a no. of joined polypeptide repeating units comprising at least 1 synthetic polypeptide of 14-40 amino acid residues including a sequence of formula (I) or (II) are new.

Ala-Lys-Val-Asn-Ile-Lys -Pro-Leu-Glu-Asp-Lys-Ile-Cys (I)

Cys-Ala-Lys-Val-Asn-Ile-Lys -Pro-Leu-Glu-Asp-Lys-Ile-Cys (II)

the polypeptides being capable of inducing the prodn. of antibodies that immunoreact with an antigen to a tuberculous **mycobacterium** when linked to a carrier and admin. to a host.

Also claimed are inocula and diagnostic kits using the polypeptides or multimers, and receptor molecules contg. an antibody combining site raised to the polypeptides.

USE/ADVANTAGE - Useful in vaccination against and detection in vitro or in vivo of infection by **Mycobacterium** tuberculosis. Immunisation with synthetic polypeptides avoids problems associated with impurities e.g. cellular debris and toxins possibly present in naturally derived vaccines. The polypeptides may be used in skin **tests** to detect infection with high specificity and may be used to circumvent cross-reactivity problems associated with known delayed-type cutaneous hypersensitivity antigens. The polypeptides may thus replace tuberculin or PPD in DCH **tests**.

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